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Detection of Ocular Changes in Avitaminosis A

Regional and Racial Relationships in Leprosy

Sporozoites of *P. lophurae* in *A. quadrimaculatus*

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Public Health Reports

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MEDICAL EVALUATION OF NUTRITIONAL STATUS [1]

IV. The Ocular Manifestations of Avitaminosis A, With Especial Consideration of the Detection of Early Changes by Biomicroscopy

By H. D. KRUSE, M. D.

This paper, in the series on the medical evaluation of nutritional status with emphasis on the recognition of early impairment, presents a preliminary report of observations on ocular changes in avitaminosis A as seen in the gross and with the biomicroscope, and particularly the biomicroscopic examination of the conjunctiva as a means of detecting early avitaminosis A.

When manifest ocular lesions of avitaminosis A were observed in a considerable number of persons in an adult group, the eye examination not only in the gross but also by biomicroscope was extended to the entire group. The principal manifestation was xerosis conjunctivae, often with mild xerosis corneae. The cases could be arranged in three main categories. In some there were gross ocular manifestations in the form of characteristic elevated spots, the so-called Bitot's spots, a feature of advanced xerosis conjunctivae. Others showed less pronounced but unmistakable gross conjunctival changes without a spot, but much more by biomicroscope. Finally, some exhibiting very little if anything grossly showed definite changes only by biomicroscope. The number of cases was sufficiently large to show all lesions as various stages in one process.

Following administration of vitamin A as specific therapy, the conjunctival lesions in nine persons have now completely disappeared, as judged by microscopic examination. In all others receiving therapy, the conjunctival lesions have markedly receded, in many to

[1] This paper is the fourth of a series from a cooperative investigation by the U. S. Public Health Service, National Institute of Health; the New York City Department of Health; the Cornell University Medical College, Department of Public Health and Preventive Medicine and Department of Pediatrics; and the Milbank Memorial Fund.

The cooperating agencies have been assisted in carrying out this investigation by the Work Projects Administration for the City of New York, Official Project No. 65-1-97-21, W. P. 24, "Medical Evaluation of Nutritional Status."

the point of near disappearance. Those not receiving therapy have shown no improvement.

DESCRIPTION OF GROUP AND PROCEDURES

One hundred and sixty-six adults, 17 to 65 years of age, were examined for grossly elevated spots. Forty-five were white females; 7, colored females; 107, white males; and 7, colored males. The white individuals were from various racial stock. None regarded themselves as sick, and all attended work regularly. All except three received incomes ranging from $52 to $95 a month.

Their eyes were examined prior to therapy. Twenty-three persons permitted only gross examination, but are included in the total for calculation of the proportion of gross spot cases. The others were examined with the biomicroscope as well as in the gross. Both types of examination were limited to the area of the bulbus exposed upon extreme rotation in many directions. In addition, the inside of the lower lid of some individuals was examined grossly, but the upper lid was not everted.

Inasmuch as specific skin lesions have been reported as an early manifestation of avitaminosis A, the skin was examined in 47 persons prior to vitamin therapy, with all grades of severity of ocular lesions. Solely for convenience, the skin examination was restricted to males among those listed for therapy. A brief history of ocular symptoms was likewise taken from these same individuals.

For ascertaining the dietary requirements of vitamin A, dietary records were taken from a selected number representative of the various stages of the conjunctival lesion, as well as those not showing it. On most of the persons with lesions, adaptometer tests were conducted before, at various intervals during, and upon completion of therapy. The results on requirements and the correlation of conjunctival lesions with dark adaptation will appear in subsequent papers.

Because of the gravity of advanced conjunctival changes, all persons with fully developed, elevated Bitot's spots were offered, even urged, to take therapy. A few refused for various reasons; they thus formed a control group for the advanced cases with spots.

Of those individuals showing gross conjunctival changes without spots and those showing only microscopic changes, only a part received therapy. Cases were graded by severity into groups from which individuals to whom therapy was offered were selected at random so that 23 of 78 persons received therapy.

Therapy was instituted in one group on September 23 and in a second group on November 1, 1940, and consisted of 100,000 U. S. P. (International) units of pure vitamin A in four capsules of 25,000 units each during the day. For the most part, the therapy was taken in

the presence of the dispenser during the 5 work days, for over the week end a supply was given to be taken home. None of the individuals were advised of the nature of their ocular condition and its probable dietary basis; no change in diet was advised, in order that there would be no suggestion or encouragement to take other or additional supplements *ex cathedra*, or to modify dietary habits.

A very few among those receiving therapy, as well as those not receiving therapy, have since become unavailable through departure and could not be further followed. Through some whim, one or two stopped therapy. In all, 61 persons are still receiving vitamin A capsules; treatment has been discontinued on the 9 now completely restored. Eye examinations have been conducted at intervals on the groups receiving and not receiving treatment; for the former these examinations have formed the basis for terminating therapy.

OCULAR SIGNS AND LESIONS IN GROSS "SPOT" CASES

Of the 166 persons examined, 65 (39 percent) had one or more manifest spots.

For the most part, the manifest spot cases include the most advanced cases. By manifest spots is meant grossly perceptible elevated conjunctival spots of distinctive color and characteristic location. Since these patients exhibited different phases of the advanced stage, the observations, both gross and microscopic, are most lucidly and succinctly presented by a composite description.

Facing bright daylight but not sunlight, most "spot" cases showed definite photophobia and lacrimation most readily elicited, however, upon examination with the slit lamp. Almost all of these patients had previously been aware of these disturbances, but it is striking that so few had noticed the spots until called to their attention.

The caruncle and plica semilunaris were usually swollen and engorged. In many instances the eyelids were swollen. The inferior fornix conjunctivae showed looseness, additional folds, and some congestion.

The vascular network in the conjunctiva was conspicuous; vessels converged radially from the canthus and fornices toward the limbus. These are large, prominent, superficial vessels from which, by close inspection, numerous lesser branches may be seen to ramify and form a fine network. This vascular pattern is distinct; but what at first seems paradoxical, the vascular plexus appears less pronounced and extensive in the eyes with most severe conjunctival involvement. Often in these instances the large vessels seem to reach only half way to the limbus.

Generalized changes varying with severity occurred in the bulbar conjunctiva. In bold outline one part may be elevated in bandlike

form above the remaining conjunctiva. There is usually wrinkling or folds, frequently along the line of apposition of the bulbar with the upper margin of the lower palpebrum, although vertical crescentic folds are sometimes seen near the inner canthus. In detail the surface shows further unevenness because the conjunctiva is raised slightly over the vessels, leaving small, shallow depressions in honeycomb pattern within the vascular outlines.

In texture the conjunctival surface may be smooth or rough; invariably it has diminished luster. Its color may be creamy, ivory, white, greenish white, whitish green, or bluish milky, according to severity. Very frequently it is a yellowish orange, taupe, or gray brown with underlying whitish green, due to association with vascularization. In appropriate light the conjunctiva of the partially advanced cases showed opalescence; sometimes it was greenish yellow, sometimes amethyst, but most often it had a silvery or galena hue.

Moreover, in seven cases pigmentation was seen as sharply localized deposits or as a narrow rim following the boundary of the limbus. This occurred only in the colored individuals, never in the white.

Depending on the stage of severity, the conjunctiva showed changes in its transmission of light. In the most advanced cases it was opaque. The color of the choroid shining through the sclera, indeed most of the vascular network, was completely obscured. Where there was opalescence, the conjunctiva was usually translucent. Frequently the superficial strata of an elevated area appeared as a transparent film, much as if a sheet of cellophane were superimposed on an opaque conjunctiva. Less advanced cases showed various degrees of translucence or diminished transparency.

That the conjunctiva is thickened may be inferred from the following gross manifestations: The irregular surface with its bandlike elevations; the very great depth to which light penetrates in the opalescent cases; the thick superficial transparent film.

Uneven contour, diminished smoothness, lackluster, and wrinkling of the surface, opalescence, localized pigmentation, thickness, changed color, and decreased transmission of light all characterize manifest xerosis conjunctivae.

The large series of "spot" cases with lesions in various gradations of development presented many intermediate stages of xerosis up to fully developed. In one zone of an eye, the changes may occasionally, in advanced stages, be of a similar degree over the entire area, but for the most part they do not occur uniformly. Because of what appears to be predilection in the site of progression, there are various topical patterns of color, thickness, and transmissibility. Frequently in the nasal zone the conjunctival thickening and opacity is limited to the third adjacent to the canthus. At the equator this may converge to a band which runs to the limbus. Thus, in the less advanced cases,

the changes may be limited to a localized segment or band, but later they may extend over the entire zone with the band forming a superstructure. The most marked involvement is near both the canthus and limbus.

The Bitot's spot occurred as part of the same process of conjunctival change. It is a small localized area where the tissue change is most advanced. In the first classification of individuals the criterion was arbitrarily adopted that the area must be elevated above its surrounding tissue in order to be regarded as a Bitot's spot. Its more pronounced color and opacity, as well as its elevation, gives it a rather well-defined border and makes it grossly distinguishable from the remaining altered conjunctiva.

Almost always the spot was located at the junction of the equator and limbus. It was most frequently triangular with the base adjacent to the limbus; but other shapes, such as oval, occasionally occurred. Its surface contour was various; flat, undulatory, ridge, and dome forms occurred about equally. In color the spot was usually white, creamy, yellow, or orange, and almost always it was opaque. It varied in the extent to which it was elevated above the rest of the conjunctiva.

Among the large number of persons the spot was observed in various stages of formation; hence, the variability in size, elevation, and color. In general, the white spots were in the earlier stage of development, while the yellow or orange were in the advanced stage. Just as the spot occurred in various stages of development, it was associated with various stages of change in the rest of the conjunctiva, but the latter was always less advanced. In the spot cases there was no gross opacity in the cornea.

Considering both the entire conjunctival lesion and the spot jointly, the degree and extent of change were usually not the same in the two zones of the same eye. In 11 persons, one spot occurred; in 9 persons, three spots occurred. When two eyes were involved, each with one spot in corresponding zones, nasal lesions were more frequent than temporal. Where spots occurred in all four zones, the nasal lesions were usually more advanced than the temporal. Here the similar zones of the individual's two eyes, e. g., the nasal zones of both eyes, often but not invariably showed a like degree and extent of change. The distribution of cases according to number of spots was as follows: one spot, 11 persons; two spots, 31; three spots, 9; and four spots, 14.

Biomicroscopic examination.—Illumination of the eye with the slit lamp brings out clearly any photophobia and lacrimation.

Upon biomicroscopic examination the large superficial conjunctival vessels were seen to ramify into medium-sized vessels which in turn branched into fine vessels; these medium and fine branches of one vessel anastomosed among themselves and with those of another to

form the network. If the conjunctiva is translucent, the vessels can be seen at several levels. Furthermore, the superficial vessels anastomose with deep vessels at various points besides the limbus. The superficial network is more extensive than the deep network. If the conjunctiva is opaque, the several strata of the superficial vessels, as well as the deep vessels, are completely obscured. The greater the impenetrability of the conjunctiva to light, the less prominent the vascular network; thus, paradoxically, the more advanced stages of the process appear to have less vascular involvement. All the superficial vessels are dilated and engorged, even in the early stages; this accounts for their gross prominence. Such deep vessels as may be seen are usually likewise dilated and engorged.

In avitaminosis A the vascular reaction at the limbus, while somewhat similar in tendency to that in ariboflavinosis, shows distinct differences. In the "spot" cases the process instead of occurring all around the limbic circumference is limited to two arcs from 8 to 10 and 2 to 4 o'clock. There is no plexiform tiering; the arcades, failing proliferation, do not extend beyond one layer. This single tier of arcades is not continuous, for here and there anastomosis has failed so that there is an interrupted pattern. Thus it appears as a vascular serration with missing teeth. Furthermore, invasion of cornea by the capillaries was slight, negligible, or absent. Corneal opacity was relatively infrequent. This is not to say that in still more severe cases the vascular reaction at limbus might not be more pronounced. In present cases, however, it was less developed and extensive there than that seen in early ariboflavinosis. Although the avitaminosis A was in an advanced stage with its most pronounced conjunctival change adjacent to the limbus, the vascular reaction there was not of the same order. Unlike that in ariboflavinosis, it was most pronounced in the superficial vessels over the conjunctiva.

Besides the vascular reaction in the grossly elevated "spot" cases, the biomicroscope reveals details of changes seen grossly, as well as those not seen grossly. The topography of the conjunctiva (surface contour) is seen to have areas of localized elevation in the form of a band, spot, or both. Wrinkling, observed grossly, is especially prominent under the biomicroscope, and is located at the line of apposition of the superior border of the lower lid with the conjunctiva bulbi. Small conjunctival cysts when situated superficially may produce a bulge, but more often they are situated deeper. Localized pigment deposits as granules or powder may be seen in some cases.

It is convenient to consider the observations on thickness and light transmission in an entire zone, and then in the spot. When part of the conjunctiva is seen to be elevated, increased thickness is inferred. Elsewhere thickness may be determined through orientation with deep vessels. Where there are several layers of superficial

vessels and opacity obscures the deeper superficial as well as the deep vessels, this may be misleading. Then some of the superficial vessels are apt to be mistaken for the deep, and increased thickness may not be recognized. In almost all instances where a spot was present, there was increased thickness of the conjunctiva over most of that zone.

In the biomicroscopic examination of the conjunctiva it is possible to recognize with slit-lamp illumination three main degrees of transmission of light: transparency, translucency, and opacity. Since the conjunctiva was always examined under tension from rotation of the eye, any diminution of transmission was minimized rather than exaggerated. A transparent conjunctiva illuminated diffusely permitted the scleral landmarks and deep vessels to be seen distinctly. Under focal illumination the conjunctiva itself appeared as a moderate suspension of fine flakes in a clear medium. When translucence prevailed, by diffuse illumination the scleral landmarks and deep vessels were seen indistinctly as through frosted glass, or were almost completely obscured. By focal illumination the conjunctiva presented a uniformly dense suspension of opaque flakes in a turbid medium; with the gradations in translucence there was considerable variability in the size of the flakes, the turbidity of the medium, and the density of the suspension. With opacity the conjunctiva by diffuse illumination was impervious to light and deep vessels were not visible. Here focal illumination added little to recognition.

Transmission of light was frequently not uniform for the entire area of a zone. For example, on the equator at the midpoint there may be punctate opacities which under indirect illumination are shown to be isolated flocculent clumps. Nor was transmission always uniform throughout the depth of the conjunctiva. The superficial layers of the conjunctiva were often more transmissive than the deep. By diffuse illumination the larger deep vessels were palely outlined, as though frost-covered. Thus, the translucence appears to be mainly in the deep conjunctival layer, or, with the upper layer transparent or translucent, the deep vessels—and probably also the deeper rami of the superficial vessels—may be entirely obscured. Here the opacity is restricted to the deep layers with their surface having a cottony appearance.

Accordingly, in classifying the transmissiveness of the conjunctiva with reference to these two strata, the following categories were used: Tr Tl, Tl Tl, Tr O, Tl O, and O O. As may be readily recognized, Tr, Tl, and O are abbreviations for transparent, translucent, and opaque, respectively. The first character of the symbol for each category refers to the superficial conjunctival strata; the second character to the deep. It should be cautioned that where the deep conjunctival layers are less transmissive than the superficial—as in Tr Tl, Tr O,

or Tl O—an extensive superficial vascular network may be mistaken for the deep; increased conjunctival thickness may be overlooked, and an erroneous conclusion reached.

In a zone with a spot, all degrees of transmission were observed in the rest of the conjunctiva. As might be expected, when the spot is in the earliest stage of development, there is least change in the remaining area; when the spot is more fully developed, there is general zonal opacity.

The spot itself, as seen microscopically, shows changes more pronounced than elsewhere in the conjunctiva. Viewed by diffuse illumination, it may exhibit scattered dots of opacity; by either focal or indirect illumination these are seen to be due to isolated clumps of flocculent material. When farther advanced the opaque mass may comprise a dense coalescence of flakes with loose aggregates around its border. Developed still more, the spot may appear either gelatinous or horny.

In a few instances where gross examination revealed a spot characteristic in all respects except that it did not project above the adjacent surface, it was possible by microscope to confirm its identity and to determine whether it was at all elevated. Then, too, in some zones the microscope detected very early opaque spots which were not grossly perceptible. Actually, both these types are true spots in the very early stages, but they are not included in the foregoing data on the number of persons with spots or on the zonal distribution of spots.

INDIVIDUALS WITHOUT MANIFEST SPOTS

The conjunctivae of 78 individuals without manifest spots were also examined grossly and microscopically. Presenting many gradations, the observed changes extended over a wide range. Profound gross alterations were seen throughout some zones, never as advanced as in most severe "spot" cases but definitely more pronounced than in early "spot" cases. The most advanced showed extensively the characteristic color changes, lackluster, and opacity. Gross nonelevated spots were observed occasionally at the junction of the equator and limbus. Some persons exhibited only the characteristic superficial vascular network in the conjunctiva. On the whole, the "nonspot" group showed less intensively any of the characteristic conjunctival changes than did the manifest spot group. Indeed, in the mildest stage little or nothing may be seen grossly; the initial changes may be revealed definitely only by biomicroscopic examination.

In practice it was convenient to classify all the "nonspot" cases according to the severity and extent of involvement on the basis of microscopic findings. Severity was judged by the degree of light transmission with transparency, translucency, and opacity represent-

ing progressively advancing stages. Where transmission differed in the superficial and deep conjunctival layers, that in the latter was regarded as decisive. Classification into the three main groups was determined by the most severe state predominating in any one zone. Then subgrouping according to extent was based on the number of zones showing preponderantly the same condition.

Certain manifestations were noted in association with particular stages. Usually light transmission was in inverse proportion to the thickness of the conjunctiva. The vascular network, as seen microscopically, is least extensive and complex in pattern in the transparent conjunctiva. It appears to be more extensive and elaborate in translucent conjunctivae than in opaque. In opaque conjunctivae the network may seem to be as inconsiderable as in transparent conjunctivae. This is because the opacity obscures most of the network which in actuality is most extensive and elaborate.

In the 78 "nonspot" persons, the microscopic observations on light transmission through the conjunctivae revealed all stages over a broad range. Seventy-seven of them had diminished transmission in one or more zones. Thus, 99 percent of the "nonspot" group showed definite signs of avitaminosis A. Twelve persons showed only marked translucence in one or two zones. Judged by less strict criteria, which excludes these 12 persons, 65 (83 percent) of the "nonspot" group had marked translucence in three or four zones, or opacity in one or more zones.

Of the 143 persons examined with the biomicroscope, 45 percent had manifest spots (gross) and another 54 percent had distinct characteristic microscopic changes. By the method of classification which includes grouping of the "nonspot" cases according to the degree of light transmission, 45 percent of the persons had one or more spots, 31 percent had one or more opaque zones, and 23 percent had one or more markedly translucent zones as determined by microscopic examination. It should be noted that Bitot's spot is merely one stage in manifest xerosis conjunctivae. In some of the "nonspot" group, among a number of those presenting opaque zones upon microscopic examination, the xerosis was of such severity that it was also grossly perceptible.

CHANGES ON THERAPY

Upon administration of 100,000 I.U. vitamin A daily to both "spot" and "nonspot" cases, regardless of severity, the initial changes detectible by microscope were the same. There was diminution of engorgement in the superficial network with vessels still dilated. The circulatory stream did not fill the vessel and its flow was slow; then there was granular circulation followed by beaded or empty

vessels. The latter were seen as shadow vessels. With this retardation in flow or disappearance of the stream, the vessels diminished in size. In most instances these vascular changes took place first in that half of the conjunctiva which borders on the cornea. Soon thereafter the entire conjunctiva, which may have been translucent or opaque, became gradually thinner and more transparent. With diminution in thickness of the conjunctiva, cysts and superficial wrinkling are not infrequently seen as transient manifestations. The clearing in the medium advances while recessive changes in vessels are continuing, yet vessels may seem more numerous because many previously obscured by opaque medium now become visible. Gradually the spot diminishes in size, becomes perceptible as an opacity only by microscope, and finally disappears. If the treatment is complete, the conjunctiva becomes smooth, thin, lustrous, much less vascularized, and highly transparent or very slightly translucent.

In persons with gross lesions, several weeks after beginning repair had been followed by microscopic examination, signs could also be recognized by simple inspection. Perhaps the earliest improvement grossly perceptible was in lessened photophobia and lacrimation. Later it was noted that the conjunctiva had changed from opaque white to translucently bluish, at first slight and only in a small area, then gradually increasing in extent and completeness. The decreasing thickness and increasing clarity of the conjunctiva permit the choroid shining through the sclera to be seen. For a time Bitot's spot may appear more prominent because its borders are more sharply outlined and its opacity is cast into sharper contrast by the clearing in the adjacent, somewhat less severely affected conjunctiva. Gradually the spot diminishes in size and disappears. The swelling in the caruncle and lids recedes. Finally, upon complete recovery, the conjunctiva has a bluish-milk shade and has taken on a noticeable luster and sparkle which enliven the eyes and impart an animated expression to the face.

It should be noted that the criteria of complete recovery are rigorous since they are based on microscopic observations: slight translucency and thinness of the conjunctiva with inactivity in or absence of an excess vascularity. After receiving therapy for 8 months, one person with spots has been completely restored and discharged. In all others with spots, the conjunctiva has become less vascular, thinner, clearer, and more lustrous. The spots are much diminished in size, in many no longer grossly elevated, in some detectible only by microscope. Of the persons with "nonspot" lesions, eight have been fully restored and discharged. Naturally, since the "nonspot" lesions are usually less severe, more in this group were among the first to show

complete recovery. Nevertheless, they have required not less than 6 months' intensive therapy.

In both groups those who have not received therapy have shown no improvement.

Following the full recovery of those still receiving therapy, there will be a more complete report.

The results of the adaptometer tests, under rigid conditions of test and with specially calibrated instruments, will be published soon in a preliminary report. At this time it may be said that only a few very high values were found in the total range for the entire group. Not all persons with most advanced xerosis showed high levels, nor were high levels restricted to those with most pronounced xerosis.

DISCUSSION

The ocular manifestations of avitaminosis A are xerosis conjunctiva, including Bitot's spot, and xerosis corneae with subsequent corneal turbidity, ulcer, and keratomalacia. There is a very extensive bibliography dating back over 100 years on the nomenclature, etiology,and pathogenesis of the conjunctival and corneal changes, as well as their interrelation, but its presentation will be reserved for a later paper. Yet it is worth while to mention here that all these manifestations in the order enumerated are regarded as successive stages of one process.

Since the present study pertains only to the initial stages, it is appropriate to cite briefly some of the original observations on the conjunctival lesions. Although the first description is usually attributed to Bitot (*4*) in 1863, Cohn (*5*) cites 60 prior references to the condition dating back to 1803.

During this time it was known by various names. Some of these, such as xerophthalmos (*6*), xeroma (*7*), conjunctiva arida (*8*), and dry conjunctiva (*9*), expressed the dryness so often present in the pronounced stage.

Several authors preferred to stress the primary nature of the lesion. Accordingly, from its histogenic character, they denoted it under the descriptive names of cuticular conjunctiva (*10*), Ueberhautung der Conjunctiva (*11*), Hautbildung der Bindehaut (*12*), skinning over the conjunctiva (*9*). These terms are highly expressive of its histogenic nature and gross appearance, what is today called the metaplastic character of the epithelium.

Then von Ammon (*13*), more concerned with differentiating its etiological independence of an inflammatory process than in denoting its essential character, proposed the name of xerosis conjunctivae. In a footnote, he explained: "Xerosis (ἡ ξηρωσις), das Trocknen, Austrocknen. Der Herausgeber hofft, dass dieser Name durch die Beschreibung und Charakterisirung der Krankheit sich rechtfertigen

wird. Er hat die bekannteren Wörter, Xerophthalmos oder Xeromma (v. ξηρος und ὄμμα), deshalb nicht gewählt, weil die Grichen, da, wo sie dieses Wort gebrauchen, hiermit die in Folge der Entzündung der Bindehaut oder anderer Theile des Auges entstehende Trockenheit dieses Organs bezeichneten." But the choice was not fortunate inasmuch as it was still vague and misleading.

Later Bitot (*4*) described the conjunctival lesions as epithelial strata or plaques assuming various shapes, but he gave them no name. Subsequent to his publication, several of his contemporaries referred to them as Bitot's spots, a name which has since gained some currency.

At the present time there is no satisfactory nomenclature expressing the true nature of the lesion. Unfortunately, it still retains the designations xerophthalmia and xerosis conjunctivae which are open to misconception because dryness is not its primary or most significant characteristic and is recognizable only in pronounced cases. Moreover, xerophthalmia is not specific for the conjunctival stage since it includes xerosis corneae as well as xerosis conjunctivae.

To some extent Bitot's spots are mentioned in the literature, but such an eponymic designation is not to be recommended. Besides, it applies only to a very particular stage of the conjunctival lesion. Of the three terms still in vogue, xerosis conjunctivae is perhaps the least objectionable to denote the conjunctival lesion, but it should carry a connotation of the fundamental nature of the lesion.

Xerosis conjunctiva, and the more advanced stage xerosis corneae, were reported in association with a series of diseases and were attributed to numerous causes. Within 2 years of Bitot's observation, Gama Lobo (*14*) asserted that xerosis occurring in Brazilian slaves resulted from lack of suitable and sufficient food. In the next year Blessig (*15*) noted that the xerosis appeared preponderantly during the 7-week Lenten fast and receded thereafter. He insisted that it was the consequence of a nutritional disturbance which was not simple inanition, and suggested lack of nitrogenous substances. Calling attention to the severe disturbance of the general nutritive condition so frequently observed with the eye lesions, Förster (*16*) in 1877 inclined to the view that "nutritive deficiency" was responsible for the ocular changes, comparable to such trophic disturbances as decubitus and diabetic gangrene. Shortly thereafter de Gouvêa (*17*) declared that xerophthalmia is a natural consequence of the general nutritional disturbance caused by chronic progressive anemia which resulted in part from heavy labor and an insufficient and deficient diet. In the same year Thalberg (*18*) reported the occurrence of keratomalacia in infants nursed by mothers who gave sufficient milk but were anemic or debilitated by prolonged fasting. Likewise, Schoeler (*19*) in 1887 observed the ocular lesions in adults who were on restricted or unbalanced diets.

From 1866 to 1904, 12 reports appeared on the successful use of liver or cod-liver oil internally for xerophthalmia (*20*). In treating more than 1,500 infants with xerosis conjunctivae, Mori (1904) (*21*) found immediate and specific response to cod-liver oil. Since their diets contained little fat, and they responded to liver oil, he attributed the ocular lesions to inadequate fat. He advanced this hypothesis despite his lack of success with sesame or olive oil.

In 1906 Falta and Noeggerath (*22*), feeding rats on a "purified" diet, noted the development of a conjunctivitis in the course of their general nutritive decline. Reproducing these results in a further investigation of this possible relationship between the conjunctival disease and diet, Knapp (*23*) in 1909 drew the interesting conclusion that the eye disorder was due to a specific dietary deficiency of an unknown substance. Then came McCollum and Davis' (*24*) demonstration that growth was not possible in rats restricted to a standard ration unless a substance contained only in certain fats (fat-soluble A) was included. Shortly, Osborne and Mendel (*25, 26*) pointed out that inflamed and purulent eyes appeared in animals on diets deficient in the fat-soluble vitamin, one source being cod-liver oil, and disappeared upon administration of it.

Whereas the preceding observations revealed a deficiency of fat-soluble A as the cause of an eye disease but did not identify the latter with xerophthalmia, other investigations showed that the ocular disease induced experimentally by a deficient diet was really xerophthalmia, but did not recognize and identify the missing dietary factor as fat-soluble A. Using a diet complete in calories and known constituents but deficient, as they knew, in certain other unidentified indispensable substances, Freise, Goldschmidt, and Frank (*27, 28*) asserted that they had experimentally produced keratomalacia. They placed it among the deficiency diseases, but their experiments did not permit them to characterize the deficiency.

Impressed by the low fat content in the diets of his xerophthalmic patients and the striking efficacy of cod-liver oil in an epidemic in Denmark during World War I, Bloch (*29*), though cognizant of McCollum's results, subscribed to Mori's theory of fat deficiency as the cause of the eye disorder. McCollum and Simmonds (*30*) thereupon enunciated the view that xerophthalmia in human beings and in rats was analogous, representing a deficiency in vitamin A. They said: "We feel confident that these cases of xerophthalmia reported by Mori and Bloch should be looked upon as a 'deficiency disease' not hitherto recognized in its true relation to diet. It is not, as these authors believe, a 'fat starvation' which produced the condition, but a lack of the unidentified dietary factor, fat-soluble A, which occurs in just those foodstuffs which they observed to possess curative properties."

Night blindness is another ocular manifestation reported as appearing in avitaminosis A. Literally it is failure or imperfection of vision at night or in dim light. There is an older and more extensive recorded history for night blindness than for xerosis. Among the views on its etiology, the nutritional was based on dietary inquiries or observations on effective therapeutic agents.

In old Chinese medicine, chicken or sheep liver was highly recommended as a specific for night blindness; and among the home remedies, chicken-liver extract in honey was popular (*31*, *32*). In 1859 Graefe (*33*) designated insufficient and poor food as a contributory factor in its causation. Following Bitot's contention that xerosis and night blindness were associated as parts of the same process, it might be expected that both would be attributed to the same cause and that therapy found effective for one would be used for the other. But, in the main, developments in views on their cause did not proceed in parallel.

Some of the early investigators who put forward the hypothesis of a nutritional etiology of xerosis did not mention any associated night blindness, nor even suggest that the same cause might be responsible for both (*16*, *18*, *19*). On the other hand, several of their contemporaries reporting that night blindness appeared under conditions of poor nutrition, as in prisons (*34*, *35*) and after long fasts (*36*), presented it as an independent entity. From 1863 to 1910 there appeared a series of reports on the beneficial effects of cod-liver oil or liver for night blindness; in one or two xerosis was mentioned but with skepticism or uncertainty over any relationship to night blindness; in most, xerosis was not mentioned; in some, scurvy was cited as a significant associated manifestation (*37*, *20*). Epidemic night blindness was stated by a few to be a consequence of faulty diet, particularly an imbalance (*37*); one specified fat deficiency (*38*).

It is true that Blessig (*15*) in 1866 charged both xerosis and night blindness to a nutritional disturbance occasioned perhaps by a deficiency of nitrogenous substances. Krienes (*37*) in 1896 attributed concurrent essential night blindness and xerosis to the same causes, of which one was nutritional disturbance. Groenouw (*39*) in 1904 mentioned the simultaneous occurrence of the two signs on long voyages where the diet was unsatisfactory. Furthermore, de Gouvêa (*17*) in 1883 and Mori (*21*) in 1904 reported that both conditions responded to cod-liver oil. Accordingly they stated that the two manifestations had a common cause; the former suggested improper and insufficient food; the latter specified a fat deficiency. These were clear exceptions to the trend to consider night blindness apart from xerosis.

Even during the period from 1913 to 1917 when vitamin A was discovered, when the occurrence of xerophthalmia in A-deficient

animals was observed, and when xerosis in persons was found to be a manifestation of avitaminosis A, any relationship of night blindness to these developments was not at once demonstrated. Perhaps the reason lies in the course of events peculiar to night blindness. Very early it was reported as occurring alone and also in association with numerous diseases. In classifying its appearance under many circumstances the earliest distinction was between idiopathic or epidemic and symptomatic. In 1881 Parinaud (*40*) suggested that night blindness is dependent on a disturbance of the visual purple in the retina. Treitel (*41*) in 1885 concluded that it is characterized essentially by a disturbance in dark adaptation. In turn, this was attributed to involvement of the visual purple in the rods.

With the development of several instruments, dysadaptation was found to result from many circumstances; and all the while the classifications of night blindness increased in number and kind. Commenting on the unsuccessful attempts to unify the concepts of night blindness, Birch-Hirschfeld (*42*) summed up the status in 1917: "The chief difficulty in explaining the nature of night blindness rests on the fact that we are dealing with a symptom rather than a uniform disease produced by a particular etiology." He presented a classification based on 11 causes, each with a different mechanism affecting visual purple. Thus it came to be believed that there were several kinds of night blindness. Acute epidemic or essential night blindness was regarded as due to dietary deficiency. During World War I, however, there were epidemics attributed to nondietary factors. Furthermore, it was pointed out that night blindness and dysadaptation were not synonymous, that disturbance in the transmissive mechanism, apart from the receptive tissue, could bring about night blindness by preventing effective operation of the visual purple.

In 1915 Wietfeldt (*43*) suggested that essential or epidemic night blindness might be due to a lack of vitamins. Upon curing this form with carrot juice or liver, Zak (*44*) in 1917 stated that it was a manifestation of avitaminosis, although his studies did not permit him to decide whether it was an independent disease or a symptom of scurvy. Hift (*45*) laid great emphasis on the concurrence of night blindness and scurvy. At the same time Birch-Hirschfeld (*42*) likewise specified vitamin deficiency as one of the primary influences in the pathogenesis of night blindness, citing scurvy, beriberi, and keratomalacia as examples without identifying the relation of night blindness. In 1923 Popovitch (*46*) suggested that it resulted from a deficiency in the fat-soluble vitamin since therapeutically active substances were rich in it. By testing the ability of rats to jump off a table in a dim light, after previous exposure to bright sunlight, Holm (*47*) demonstrated that vitamin A deficient rats had developed a well-defined night blindness. The administration of vitamin A to them resulted in a

disappearance of symptoms. At the same time Fridericia and Holm (*48*) reported that vitamin A deficient rats placed in the dark after exposure to light showed a retarded regeneration of visual purple. Thus one form of night blindness, with dysadaptation due to impaired regeneration of visual purple, was linked with avitaminosis A.

Very largely on the basis of the latter studies (*47, 48*), night blindness came to be regarded also as the earliest sign of avitaminosis A. Of the delay in regeneration of visual purple, Fridericia and Holm said: "This symptom is an early one, being manifested as soon as the growth of the young rat stops and earlier than the onset of pronounced xerophthalmic symptoms." Even more emphatic was Holm: "The hemeralopia in the experimental-rats could be detected soon after the alimentation on food without fat-soluble-A had begun, * * * *at a stage where it was impossible to perceive any other sure signs of avitaminosis* except a slight failure to increase normally in weight."

This view that night blindness is the earliest sign of avitaminosis A gained ready acceptance in clinical medicine. In a textbook (*49*) on the clinical manifestations of avitaminoses, it is said: "* * * bilden sie eine besondere Trias, die allerdings beim gleichen Individuum nicht immer gleichzeitig, sondern meist in einer bestimmten zeitlichen Reihenfolge: Hemeralopie- Xerophthalmie-Keratomalacie, angetroffen wird." Several reasons probably contributed to this acceptance. Although originally the simultaneous presence of two or all three of the signs in the same person finally came to be noted there was no common agreement at that time on the sequence of events. Subsequently knowledge concerning night blindness developed separately. Within the past 25 years there have been numerous recorded epidemics of night blindness. In that time there have been few or no reports on any high incidences of xerosis conjunctivae, although there have been recorded outbreaks of xerosis corneae and keratomalacia in which xerosis conjunctivae alone, as the initial change, must certainly have been present earlier. Emphasis, however, was placed on the more severe stage, keratomalacia; indeed xerophthalmia more and more came to connote more strictly the corneal stage. As an advanced stage, its subsequence to night blindness was not questioned. Furthermore, night blindness was detected because of patient's complaint; but in xerosis conjunctivae, since visual acuity is not markedly affected, the patients are usually not concerned over the symptoms until inquiry directs attention to them.

When night blindness was said to be the earliest sign, it came to mean that it is a manifestation of mild avitaminosis A, either too short in duration or insufficiently severe in degree to produce xerophthalmia (*50*). This view gave fresh impetus to tests for dark adaptation as a means of detecting avitaminosis A, particularly the subclinical stage. With technical improvements it became possible to measure

small deviations in dark adaptation. Since manifest night blindness was regarded as the earliest ocular sign of avitaminosis A, these small changes were understandably interpreted as a still earlier stage of the disturbance. All this has strengthened the notion that night blindness, or dysadaptation, is the earliest change.

Nevertheless, when the entire record of events is carefully consulted, it is proper to raise three questions: Is night blindness a specific manifestation of avitaminosis A? Can night blindness result from vitamin A deficiency alone? Is night blindness the earliest sign of avitaminosis A? Each has a bearing on the usefulness of the adaptometer as a means of detecting subclinical avitaminosis A. The first two questions, however, may be considered jointly.

By almost every investigator of epidemic night blindness, from the very earliest to the more recent, its onset has been attributed to overexposure to bright light (*4, 17, 33, 35–40, 42, 47, 48*). Its occurrence predominantly among workers exposed to the sunlight for long hours, day after day, as in the fields and at sea, was at once suggestive and convincing. In accord with it were the observations that night-blind patients experienced no difficulty in seeing in early morning although it was much darker than in the evening (*17, 48*). Throughout the course of expanding and shifting views on the etiology of night blindness, investigators continued to lay stress on light; most of them designated it as the determining or precipitating influence. Deficient diet was regarded until recently only as a contributory factor. Other evidence added support to the view that light was a significant influence. For many years the standard treatment for night blindness was confinement in a dark room for 48 hours, or the use of dark glasses. The prompt efficacy of this treatment gave substance to the views about the influence of light in the causation of night blindness.

On the experimental side, it should be recalled that Fridericia and Holm succeeded in inducing night blindness and dysadaptation in vitamin A deficient rats only after exposing them to intense sunlight for several hours daily over a period of several weeks and then to artificial light for 20 minutes prior to the test (*47, 48*). Holm declared (*47*): "Hemeralopia does not develop through lack of fat-soluble-A-vitamin alone; *it is necessary also that the individuals be much exposed to light.*" It may well be that actinic rays have an aggravating effect on avitaminosis A; it should be borne in mind that such a reaction has been noted in ariboflavinosis and pellagra. In any event, all these observations are pertinent to any consideration of the prevalent view that vitamin A deficiency alone produces night blindness as a specific manifestation. They also raise the question whether the present procedure in the tests for dysadaptation would permit detection of it in the subclinical stage.

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The place of night blindness in the sequence of ocular manifestations is a matter fundamental to the early detection of avitaminosis A. When all circumstances are taken into account, it is quite possible that night blindness may not be the earliest ocular change. Reexamination of the very early records brings out the uncertainty in the matter and at the same time indicates the advisability of giving fuller consideration to xerosis conjunctivae. It is well to recall that 100 years ago clinicians seeking signs for early detection of the syndrome debated this very question of whether night blindness or xerosis conjunctivae is earlier. There was marked divergence of opinion, but the evidence supported equally well, if not preponderantly, the priority of xerosis. For one thing, in Bitot's series of cases, the conjunctival spots occurred without night blindness. Besides, in some cases night blindness appeared only after the xerosis was far advanced. Bitot regarded xerosis as the herald of night blindness.

Although the recorded epidemics of night blindness in which xerosis was not mentioned have doubtless favored acceptance of night blindness as the earliest manifestation of avitaminosis A, the view really hinges on the animal experiments of Fridericia and Holm (*47*, *48*). It should be noted that when they stated (*48*) that dysadaptation preceded pronounced xerophthalmic symptoms, they meant that dysadaptation preceded corneal involvement, which is an advanced or late stage. Furthermore, when Holm (*47*) stated that night blindness developed in the rats before any perceptible signs of avitaminosis except retardation in growth, he was judging by three signs not recorded for man: enophthalmus, loss of ciliary hair, and a peculiar lacrimal secretion. He did not mention looking for xerotic changes in the conjunctivae other than to state that because of physical conditions it is impossible to produce Bitot's spots in rats. Certainly on the basis of neither study can it be said that night blindness precedes xerosis conjunctivae. In fact, the observations, both clinical and experimental, would seem to cast some doubt on the validity of the prevalent view that night blindness is the first ocular sign of avitaminosis A.

Present-day work does not dispel this doubt. In studies on adaptation with sensitive equipment, often the validity of the data on avitaminosis A has not been supported by therapeutic evidence. In other instances it has been shown that small differences supposedly representing improvement from vitamin A therapy were probably learning responses or instrumental artefacts (*51*, *52*, *53*).

This background would seem to warrant reopening the question of whether xerosis or night blindness is the earlier manifestation. While the old observations serve to revive the issue, they cannot settle it. Then both conditions were diagnosed only in their advanced stages and in a way—xerosis by gross examination and night blindness by

history—which is inconclusive on the point of priority. For this it is necessary to have observations with sensitive instruments on early dysadaptation and xerosis, noting their concurrence or order of appearance. With the calibrated adaptometer and the biomicroscope, this became possible. In the present study dysadaptation did not precede the xerosis conjunctivae. Indeed, dysadaptation was not specifically correlated with the degree of conjunctival change.

It is generally accepted that characteristic lesions in the eye are not the only changes in avitaminosis A, nor are they regarded as the first. However, the intimation that skin lesions, under such varied names as follicular hyperkeratosis, phrynoderma, and xeroderma, represent the initial manifestation (*54*) finds no support from histopathological studies on experimental animals. In the "spot" cases of the present study, only occasionally were possible dermal lesions noted; then they were so indefinite as to be questionable. None were seen in persons with less severe eye lesions. In the entire series, therefore, gross cutaneous did not precede ocular changes.

In suggesting biomicroscopic examination of the eye as a means of detecting early avitaminosis A, it is not meant to imply that the ocular lesion is the sole, the first, or the most important change. Xerophthalmia is not synonymous with avitaminosis A. Histopathological examinations on both humans and animals have shown that avitaminosis A is characterized by widespread epithelial changes throughout the body, for example, the respiratory, paraocular, and renal, as well as the ocular organs (*55*, *56*, *57*). Wolbach and Howe (*56*) have stated that xerophthalmia is not the earliest manifestation of avitaminosis A in the rat. For human beings there is very little evidence on what is the initial site and the sequence of sites undergoing change.

Nevertheless, among the organs showing early change, the eyes are a favorable site for detecting vitamin A involvement, for they are accessible to observation or test. There is another point of advantage: the initial lesion in the eye occurs in the conjunctiva. Inspection for gross changes, including Bitot's spots, may be used in screening advanced cases, which may be subgrouped, if desired, according to the number of zones affected. Biomicroscopic examination detects subgross changes of all gradations which may be classified according to severity and extent. Hence, by combined gross and microscopic examinations, it is possible to determine all stages of xerosis and thus to grade the avitaminosis A.

Especially does the biomicroscopic examination of the bulbar surface present several additional advantages: (1) it shows the early changes in the conjunctiva—site of the initial ocular lesion in avitaminosis A—that are not visible grossly; (2) it is a rapid, convenient, and objective method for detecting the very early avitaminosis A;

(3) it permits a simultaneous examination of the limbus and cornea for early ariboflavinosis, from which avitaminosis A is easily differentiated; (4) it provides a much-needed means for ascertaining the dietary requirements for both vitamin A and riboflavin.

In the present study, the examination of conjunctivae both grossly and biomicroscopically shows a high prevalence of avitaminosis A in this low-income group. It is so high as to seem at first glance almost incredible, but it is substantiated on several grounds.

In reporting on a national dietary survey Stiebeling and Phipard stated (*58*): "Taking 6,000 International Units per day as the allowance for the adult man, * * * it is estimated that the lowest 25 per cent of the diets [for all of the white families represented by the study] furnished 2,000 or less International Units a requirement unit a day, and the lowest 75 per cent, less than 4,500 International Units a day." In the cities of the North Atlantic region, including New York City, they found that in the group with a weekly per capita expenditure for food between $1.25 and $1.87, 67 percent had less than 2,000 International Units, 20 percent had between 2,000 and 3,999 Units, and 9 percent between 4,000 and 5,999 Units. At least 90 percent were thus receiving less than the estimated required amount of vitamin A. In the present study, the prevalence of avitaminosis A in the comparably low income group was more than 90 percent.[2] These figures strikingly bear out the dietary data while the latter, in turn, account for the high prevalence, suggesting that dietary deficiency was largely responsible.

In addition, it is not at all unlikely that in some instances other factors contributed to the prevalence. For example, it is conceivable that certain acute illnesses disturbing the vitamin A economy may have brought on the avitaminosis or accentuated existing lesions so that in convalescence even an abundant amount of the essential in the diet would not be sufficient for rapid restoration. With a slightly inferior diet, recovery would not be complete for an indefinite period.

Furthermore, with manifest conjunctival lesions in 45 percent of the persons, a sizable number with less pronounced changes visible only with the biomicroscope would be expected. But above all, the response of the affected persons to the specific therapy attests to the actuality of avitaminosis A in so large a proportion of the group.

Upon administration of therapy, recession is similar in type to that in ariboflavinosis: obliteration of vessels and dissipation of opacities. The striking feature, however, is the very long period required for complete recovery, a matter of months even with therapy of high

[2] A lower prevalence would be expected in higher income groups. Upon examination of 25 adults in a medium income group, 16 showed definite conjunctival changes. Five persons in the group had gross spots. It is more than likely that avitaminosis A is one of the more commonly occurring deficiency diseases and is present in a considerable proportion of the population.

potency. This is reasonable considering that when the eyes show such profound change, many epithelial structures throughout the body are known to be simultaneously affected. Restoration of all this epithelium takes time.

These results indicate that complete recovery from this deficiency disease is not so rapid as is popularly reported. This protracted recovery, even with high dosage of vitamin A, also casts a significant light on therapeutic practice in avitaminoses. Currently it is often asserted that adequate diet corrects deficiency diseases. In a sense this is true if time is no consideration. But if therapy of high potency brings about complete recovery only after an extended period, an optimum diet might be expected to require a very much longer time. It seems necessary to take the view that persons affected with deficiency diseases need intensive specific therapy for most rapid recovery. Obviously, an optimum diet should be instituted for its supplementary nutritive value, its protection against outbreak of other deficiencies, and for establishment of satisfactory dietary practice by the patient. Then when therapy is withdrawn upon recovery, the satisfactory dietary habits suffice for maintenance.

The use here of 100,000 I. U. of vitamin A daily is not to be construed as a recommendation or precedent that this amount is necessary for maximum rapid therapeutic results. In the present study it was essential to administer an amount that would ensure maximum response. It is certain that tissues have critical rates of response and that doses in excess of the amounts satisfying those rates have no further effect. It is common experience that effective therapeutic dosage for an avitaminosis is at least five to six times the maintenance requirement. Actually, therefore, it may be that daily levels of vitamin A between 25,000 and 50,000 I. U., for example, will be found sufficient to produce maximum therapeutic response. That is to be determined.

SUMMARY

Of 143 persons in a low income group, 45 percent had gross and another 54 percent had microscopic ocular lesions characteristic of avitaminosis A. The ocular condition was xerosis conjunctivae.

Following administration of vitamin A as specific therapy to a part of the group, the conjunctival lesions in nine persons have now completely disappeared, as judged in all instances by biomicroscopic examination. In all others receiving therapy, the conjunctival lesions have markedly receded to the point of near disappearance.

In all cases the striking feature is the very long period of time required for complete recovery, a matter of months even with therapy of high potency.

Those persons not receiving therapy have shown no improvement.

It is suggested that xerosis probably precedes night blindness as an early sign of avitaminosis A.

For detection of early avitaminosis A in surveys, the biomicroscopic examination is recommended as a simple, convenient, objective method. When it is combined with gross examination, all degrees of xerosis may be graded according to severity and extent.

The marked prevalence of avitaminosis A in this low income group, objectifying and validating previous dietary data, suggests its relatively frequent occurrence in the population at large.

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REGIONAL, RACIAL, AND FAMILIAL RELATIONSHIPS IN LEPROSY IN THE UNITED STATES[1]

By W. Lloyd Aycock, *Director of Research, Harvard Infantile Paralysis Commission,* and James W. Hawkins, *Assistant Surgeon, United States Public Health Service*

In the first half of the nineteenth century, when no one of the factors in the causation of infectious disease was given preference

[1] From the Department of Preventive Medicine and Epidemiology, Harvard University, Boston, Mass. Financed by the Harvard Infantile Paralysis Commission and a grant from the Commonwealth Fund.

over others, remote circumstances were freely included with contagion. Thus, Joseph Gallup wrote of certain epidemic infections in 1815, "If diseases of this class are propagated by a contagious principle, it is of a singular sort, not subject to the laws of any known contagion." And he "assigned their origin * * * more to remote influences affecting the system which increase liability to disease."

With the development of the science of bacteriology, emphasis turned toward the immediate circumstance of exposure to the infectious agent as the more important determinant in the occurrence of disease, and the mode of spread became the central idea in epidemiology. But, with increasing knowledge of such phenomena as latent and subclinical infection and healthy carriers, many instances are now seen where the patterns of virus dissemination and disease distribution do not coincide. More or less remote factors are again recognized as important determinants in the limited or selective occurrence of disease in those exposed to the infectious agent.

Concepts in leprosy have followed these changing trends in thought in the epidemiology of infectious diseases. The doctrine of hereditary transmission, promulgated by Danielssen and Boeck, prevailed from 1848 until the discovery of the Hansen bacillus in 1874. The viewpoint of the contagionists then came to the forefront and nas remained predominant, the failure of the disease to follow ordinary lines of contagion being attributed to supposed variations in the degree or duration of exposure to the infectious agent. For example, the well-known familial tendency of the disease has been ascribed to "prolonged and intimate exposure." But, with the recognition of the tendency of leprosy to remain restricted to certain regions, races, and families for long periods of time, beyond anything which could be explained by corresponding restrictions in exposure, doubt has been thrown upon the belief that contagion is the major determinant in the distribution of the disease, and the role of more remote influences is again being considered.

Hereditary susceptibility, a factor which has long been believed to be concerned in the occurrence of leprosy in those exposed, has been the subject of previous communications in connection with certain foci of the disease on the North American continent (*1*, *2*). This paper presents a study of certain regional, racial, and familial relationships of leprosy throughout the United States with similar implications. The data [2] comprise information concerning 927 admissions to the U. S. Marine Hospital, Carville, La., during the 18-year period from February 1921 (when the Louisiana Leper Home was acquired by the Federal Government) to December 18, 1939, including the place and date of birth of the patient, race, and sex, and place

[2] Data kindly furnished by Dr. H. E. Hasseltine, Medical Director, U. S. Marine Hospital, Carville, La.

and date of admission. Since names of patients are not available, this study is restricted so far as familial occurrence is concerned.

Admission to the hospital rests upon State regulations, and, although these differ in the various States, it would seem likely that the general consensus in regard to segregation is such that the number of patients at Carville is probably a fair index of the distribution of the disease in the United States (although estimates give varying proportions, down to one-half of those that actually exist).

LEPROSY IN FOREIGN-BORN PERSONS

The 430 foreign-born leprosy patients have been recorded as of the State from which they were admitted. Such an allocation, it is realized, may not be a complete representation of case distribution, since it is probable that a considerable period elapsed between the development of the disease and admission, during which time many of these immigrants doubtless moved from place to place, but it is enough to show that cases of leprosy have been introduced into many parts of the United States, and in greater numbers at certain points of immigration (fig. 1).

The more important racial and geographic groupings within the United States of the foreign-born patients are shown in table 1. That they represent largely importations is indicated by the fact that they come mostly from countries where the disease is known to be prevalent.

TABLE 1.—*Regional and racial distribution of foreign-born leprosy patients in the United States*

State from which admitted	Country of birth															
	Mexico	West Indies	Philippines	China	Greece	Hawaii	Italy	Russia	Spain	Portugal	Germany	Canada	Finland	Norway	Other	Total
Arizona	4															4
California	60	4	35	17	3	12		1	3	2					14	151
Colorado	6															6
Florida		9							1							10
Illinois	8	1	3	2				1							2	17
Louisiana	2						4	1				1			1	9
Massachusetts		2	1	1	3		3	1		3					6	20
Michigan	4			2	2		1								3	12
Minnesota			1		1							1	2	1		6
Missouri	1			1	1				1						2	6
New Jersey		3			1					1					1	6
New York	1	35	4	9	8	3	6	6	2	1	1	2		1	21	100
Oregon			1	1	1	1										4
Pennsylvania			1				1	1	1						2	6
Texas	38						1								1	40
Virginia		2	1												1	4
Washington			7											1		8
Wisconsin					1						1					2
Other States	5	1	2	1	3	1	1	1	2		1		1			19
Total	129	57	56	34	24	17	17	12	10	7	3	4	3	3	54	430

FIGURE 1.—Foreign-born cases of leprosy, by place of admission.

Furthermore, their geographic distribution by nativity in this country is in accordance with immigratory expectancy. Cases of leprosy in the foreign-born population of this country would thus appear to be attributable to the more remote circumstance of origin in a foreign leprous area, and are of interest in the present connection only as possible sources of infection for cases arising in this country, which form the nucleus of this study.

LEPROSY IN AMERICAN-BORN PERSONS

The data include 497 cases of leprosy among persons born in various parts of the United States. For epidemiologic study, two groupings have been made: (1) Those born in and admitted from the same State, and designated "stationary cases;" (2) those born in one State and admitted from another, the so-called "migrant cases." The stationary cases probably are a more accurate index of geographic distribution, since the difficulty in setting accurately the time of infection in leprosy, with its variable and often prolonged incubation period, makes the actual place of origin of the migrant cases more uncertain.

Regional distribution.—The geographic distribution of the 396 patients born in and admitted from the same State, and hence presumably stationary, is shown in figure 2. Of this group, 370 patients were, by birth and admission, from California, Texas, Louisiana, and Florida, revealing four areas of concentration of the disease which have been designated "major foci." An additional case may also be associated with this group, a patient with a history of residence in Texas and California, although born in and admitted from a State outside the focal area.

Of the remainder, 17 patients were born in and admitted from States which are considered lesser foci, not so much because of the number of cases in this series, but because of the continued occurrence of the disease in these places for a long time prior to the period covered in the present paper (*2*, *3*, *4*). Fourteen patients were born in and admitted from the southeastern States of Mississippi, Alabama, Georgia, and South Carolina (2 of these had also resided in States considered major foci), and 3 patients were born in and admitted from the northwestern States of Minnesota and Wisconsin.

Four of the eight remaining cases give a history of having resided in a foreign country where the disease prevails. Thus, only 4 of the 396 stationary cases in the series fail to give a history of contact with a local or foreign focus of leprosy.

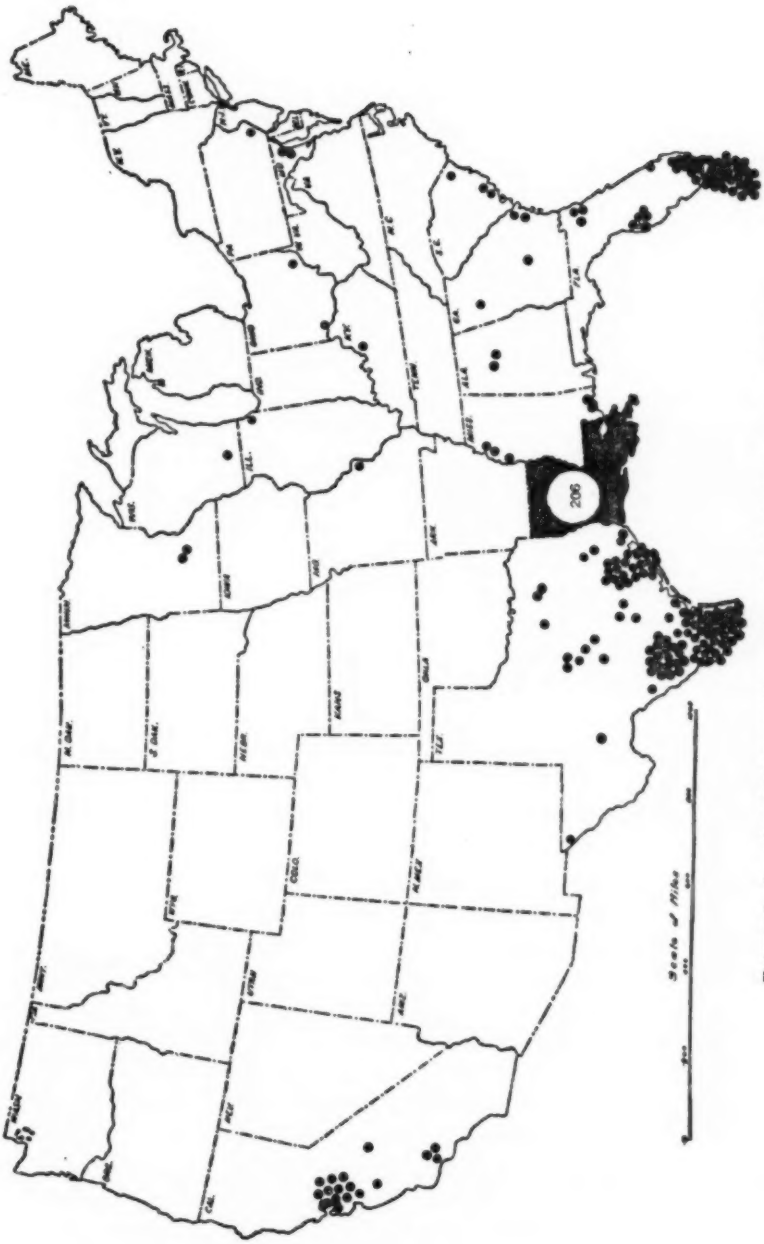

FIGURE 2.—Location of 396 cases of leprosy born in and admitted from the same State.

TABLE 2.—*Association of cases with various foci of leprosy*

	Total cases	Association with major foci				Association with lesser foci		Association with foreign foci	Sporadic cases
		Birth and admission	Birth only	Admission only	Residence only	Birth and admission	Birth only		
Born in and admitted from same State	396	370	0	0	1	17	0	4	4
Born in one State and admitted from another	101	15	28	31	4	0	4	17	2
Total	497	385	28	31	5	17	4	21	6

The 101 cases born in one State and admitted from another are shown both by birthplace and by place of admission in figure 3. They are widely scattered when considered according to either designation, yet those with a wide dispersion according to State of birth have a high degree of association according to State of admission with the leprous foci with which the 396 stationary cases are connected, and those widely dispersed by admission show a similar association by birth.

A history of association with the major foci of California, Texas, Louisiana, and Florida is given in 78 of this group of cases: 15 were born in and admitted from these four States; 28 were born in these States but admitted from elsewhere in the country; 31 were admitted from one of these foci, although born in other States; and 4 cases give a history of residence in these major foci at some time, although born in and admitted from other States. The States of Mississippi, Alabama, Georgia, and South Carolina, considered lesser foci, are given as the place of birth of 4 cases. Only 19 migrant cases, then, fail to give a history of association by residence, by admission, or by birth with a focus of the disease in this country. There is a history of contact with a foreign focus in 17 of these cases, leaving only 2 which have no association with any leprous focus (table 2).

Thus, 491 of the 497 cases of leprosy in native-born persons in this series can be allocated to known areas of prevalence of the disease either in this country or abroad, leaving only 6 cases which may be taken to represent the sporadic occurrence of the disease within the United States. Histories of these cases are as follows:

Case 1.—Negro male, admitted from Philadelphia, Pa., August 31, 1928, aged 57 years. This patient could not give a very satisfactory history, but it could not be learned that he had ever been out of Pennsylvania. He has died.

Case 2.—Male, of Italian parentage. Born in Baltimore, Md., and admitted from there on May 28, 1924, at the age of 14 years. This patient is the son of a leprous Italian-born mother and had two leprous brothers, one foreign-born and the other presumably born in the United States.

FIGURE 3.—Location of 101 cases of leprosy born in one State and admitted from another. Open circle=born; black circle=admitted.

Case 3.—Female, of German ancestry. Born in and admitted from St. Louis, Mo., March 19, 1922, aged 24 years. This woman had always lived in Missouri, though she may have gone to Illinois occasionally.

Case 4.—Female, of German ancestry. Born in Baltimore, Md., and admitted from there on June 29, 1932, aged 44 years. She lived in Norfolk, Va., for a number of years where her husband worked, but was not acquainted with any of the other patients from there, who were in the Navy. She returned to Baltimore just before the diagnosis was made. She cannot recall ever seeing or hearing of a case of leprosy prior to the recognition of the disease in herself.

Case 5.—Female, of German ancestry. Born in Kansas and admitted from Chicago, Ill., on June 13, 1937, at the age of 31 years. This patient is the daughter of case 6. Her father was of full-blood German ancestry, her mother having a mixture of Irish and American Indian ancestry (paternal) and German and some unknown ancestry (maternal).

Case 6.—Female, partly of German ancestry. Born in Lee County, Va., and admitted from Chicago, Ill., on January 19, 1939, aged 54 years. She is the mother of case 5. When she was 12 years old the family moved to Kansas, where she later married and raised a family. The mother presumably contracted the disease from her daughter, since case 5 showed symptoms 5 to 10 years earlier than did case 6.

Cases 1 and 2 are questionably sporadic and difficult to assign, because of unsatisfactory information concerning the first, and the uncertain origin of the second.

Cases 3, 4, 5, and 6, because of certain relationships between them, to be discussed, are considered in the light of one another. Geographically, they are distributed in pairs, two originating in the adjacent midwestern States of Missouri and Kansas and two in the adjacent eastern States of Maryland and Virginia. It is striking that all four are of German ancestry.

It is pertinent to recall in connection with cases 5 and 6 that our data do not include the names of patients. But the fact that two cases, one born in Kansas and one born in Virginia, were both admitted from the same city in a third State led to further inquiry, which revealed that the two patients were mother and daughter.

Racial distribution.—There is a limited correspondence in geographic distribution between the two groups of cases born in the United States and the group born outside the United States, namely, the high incidence in California, Texas, Louisiana, and Florida. On the other hand, in such States as New York, Massachusetts, Michigan, and Illinois, which have a considerable number of imported cases, there is no leprosy among the native-born population.

Racially, there is still less relationship between the native- and foreign-born cases of leprosy in the same areas. In California, we do find a proportion of domestic cases occurring in the same racial stocks as the imported cases. Texas has the largest proportion of domestic cases of the same stock as the immigrant cases, but even here numbers of cases occur in other racial groups. In Florida and

in the larger focus in Louisiana, the foreign-born and domestic cases are in different racial stocks.

The geographic and racial groupings of American-born cases thus make it evident that the introduction of leprosy from without only partially explains the existence of the leprous foci in this country. The disease may spread to individuals in the area who are of the same stock as those introducing the infection, but just as often it is associated with other racial groups living in the same area; or it may not spread at all. In no case is leprosy present in all racial stocks in the areas involved in proportion to their numbers.

The propagation of the disease, therefore, appears to be dependent in part on the presence of certain racial groups, not necessarily of the same origin as those which introduce the infection. The racial descent in the more important groups among the 396 cases born in and admitted from the same State and of the 101 migrant cases is shown in table 3, from which the general conformity in the racial composition of the two groups may be seen.

TABLE 3.—*Regional and racial distribution of leprosy among persons born in the United States*

	Racial descent																			
	French	Negro	Mexican	German	Irish	English	"American"	Chinese	Italian	Scotch	Jewish	Spanish	Dutch	Swedish	American Indian	Cuban	Norwegian	Austrian	Unknown	Total[1]
Stationary cases:																				
Louisiana	63	44	1	12	5	2	4	....	3	1	1	1	1	....	1	....	1	....	80	206
Texas	4	6	45	13	6	4	2	....	1	3	2	2	1	....	....	....	....	....	25	101
Florida	....	5	....	1	2	6	4	....	....	2	....	1	....	....	....	1	....	....	29	46
California	....	....	....	2	4	....	....	5	....	....	1	....	....	....	....	....	....	....	7	17
Mississippi	....	1	....	2	....	....	....	2	....	....	....	....	....	....	....	....	....	....	2	5
Georgia	....	2	....	....	....	....	1	....	....	....	....	....	....	....	....	....	....	....	1	4
South Carolina	....	2	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1	3
Alabama	....	....	....	....	....	1	....	....	....	....	....	....	....	....	....	....	....	....	1	2
Other States	....	1	....	4	....	....	....	....	3	....	1	....	....	2	....	....	....	....	1	12
Migrant cases	7	14	5	10	14	5	5	5	1	5	3	2	2	....	3	1	....	1	36	101
Total	74	75	51	44	31	18	16	12	8	11	8	6	4	2	4	2	1	1	183	497

[1] 54 individuals of biracial stock are listed under both races.

Involvement of a single racial stock in the four sporadic cases of domestic leprosy in this series has prompted an analysis of all the cases of the disease in persons of German descent in this country. The place of admission of foreign-born cases of German ancestry, and the birthplace and place of admission, as well as association with leprous foci here and abroad of native-born persons of German descent, are indicated in figure 4.

The concentration of cases in persons of German stock in Texas coincides with the area involved in the focus of the disease there.

F
F
F
Scale of Miles
• Foreign-born
● Born and Admitted
O Born
• Admitted
---F--- Foreign Association
---➤ Associated by Residence

Although in Louisiana the main focus of the disease in another racial group is outside of New Orleans, the concentration of cases of German stock is almost entirely within this city. The remaining cases of German descent occur in less defined areas in central United States.

Regional relationships between these cases are indicated in figure 4. One patient born in New Orleans was admitted from Norfolk, Va. Case 4 of the group of sporadic cases, it will be recalled, had resided in Norfolk. Two patients, one born in New Orleans and one in Texas, were admitted from Missouri, while one born in Missouri was admitted from Texas. One patient born in Arizona was admitted from California, and two were born in and admitted from California. Three others, from Iowa, Illinois, and Ohio, respectively, had resided in foreign foci of the disease. The proportion of persons of German descent among native- and foreign-born patients, where ancestry is given, is as follows: Of 378 foreign-born patients, 6, or 1.58 percent, were German. Of 249 native patients born in and admitted from the same State, 33, or 13.2 percent, were of German ancestry; and of 58 cases born in one State and admitted from another, 10, or 17.2 percent, were of German descent.

Three additional cases, not admitted to Carville and therefore not included, have come under the observation of the writers in the course of this study: (1) A Chinese, born in China, seen in Massachusetts in 1940 with advanced lesions, diagnosed after a residence of 12 years in this country; (2) a patient residing in Louisiana, of French descent, with a history of leprosy in both parents and a sister; (3) a patient seen in California in the summer of 1940, of German ancestry, born in Missouri.

The first of these cases illustrates leprosy in a foreign-born individual coming from a known focus, living in this country in a nonfocal area, with no evidence of spread. The second case illustrates the occurrence of stationary leprosy in a focal area of the United States, in a native-born individual of the racial stock heavily involved, and of a family known to be leprous. The third instance illustrates the occurrence of a migrant case of leprosy in an individual born in central United States, of a racial stock in which a number of individuals have developed leprosy either in the area or following association with a focus of leprosy in this country or abroad.

Each of these three cases is an illustration of one of the features of the disease brought out in the study of the whole group. This conformity to the series is a further indication that regional, racial, and familial relationships of the disease shown in the whole group are not fortuitous, but are characteristics of the disease in the United States.

CONCLUSIONS

The prevalence of leprosy in certain areas in the United States appears to be dependent in part on the presence of cases as sources of infection, and in part on the presence in these areas of individuals of certain racial stocks or families.

The regional, racial, and familial relationships in certain of the cases in persons of German descent suggest a further study of familial occurrence in this and other racial groups within the United States.

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SPOROZOITES OF *PLASMODIUM LOPHURAE*, AN AVIAN MALARIA PARASITE, IN *ANOPHELES QUADRIMACULATUS*[1]

By HERBERT S. HURLBUT and REDGINAL HEWITT

Coggeshall (*1*) has recently reported the development of *Plasmodium lophurae* to the oöcyst stage in *Anopheles quadrimaculatus*. Following this lead, we have succeeded in obtaining sporozoites of this species in *A. quadrimaculatus* fed on infected ducks. All mosquitoes were kept at approximately 75° F. Dissections were made over a period of 4 to 27 days after the infective feeding. Seven out of twenty-nine dissections were positive for oöcysts and one for sporozoites. The first oöcysts were found on the seventh day and the single gland-positive specimen on the twenty-second day. The gland-positive specimen had developed an extremely heavy stomach infection, oöcysts being so numerous that they covered the greater part of the surface of the stomach. Sporozoites were few in number but most of the oöcysts had not yet developed to maturity. In normal saline the sporozoites showed slight motility, and characteristic morphology was observed in a stained preparation. Transmission of the parasite has not yet been accomplished.

In addition to Coggeshall, two other workers have reported infection of anopheline mosquitoes with avian malaria parasites, but neither of these progressed beyond the oöcyst stage. Mayne (*2*) found oöcysts of *P. relictum* in *A. subpictus* experimentally fed on an infected sparrow, and in other mosquitoes caught in a room where infected birds were

[1] From the Health and Safety Department, Tennessee Valley Authority, Wilson Dam, Alabama.

kept. Lucena (*3*) describes an experimental infection of *A. strodei* with *P. cathemerium*, but only a single oöcyst was found.

From the standpoint of certain types of laboratory research on malaria large avian hosts are desirable. However, in this country at least, no mosquito vector has been found for the species of malaria now available in large bird hosts, so far as is known to the writers. It is interesting, therefore, that development of *P. lophurae* to the sporozoite stage can occur in *A. quadrimaculatus*, although further work may show that this mosquito is not capable of transmitting the parasite.

Considerable importance is sometimes attached to oöcyst and sporozoite indices in *A. quadrimaculatus* associated with endemic human malaria. It appears, therefore, that some method should be sought to distinguish between the exogenous stages of human and avian malaria in this species, since the finding reported here tends to invalidate the assumption that all oöcysts and sporozoites which may be found are those of human malaria. Apparently very few attempts have been made to infect *A. quadrimaculatus* with species of avian malaria other than *P. lophurae* or *P. relictum*.

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COURT DECISION ON PUBLIC HEALTH

Retail food seller held liable for tularemia infection.—(Ohio Supreme Court; *Rubbo* v. *Hughes Provision Co.*, 34 N.E.2d 202, decided April 30, 1941.) In an action against a provision company it appeared that the husband of the plaintiff purchased some rabbits from the defendant's market, which rabbits the plaintiff prepared and cooked. After eating the rabbit meat the plaintiff became ill with tularemia. The rabbits were sold at a counter which was rented by the defendant to a third person, but the advertisement regarding the sale of the rabbits was by the defendant and the purchase was made without knowledge of the arrangements between the defendant and its lessee and in the belief that the defendant was the seller of all merchandise in the market. The judgment of the trial court, affirmed by the court of appeals, was in favor of the plaintiff.

When the cause reached the supreme court one of the questions submitted by the defendant for decision was whether the doctrine of agency by estoppel applied. Regarding this the supreme court said that it agreed with the court of appeals in its opinion that, when the provision company advertised the sale of rabbits in its place of busi-

ness, prospective purchasers going to the company's place of business had a right to assume that the company was selling those rabbits through its employees, in the absence of knowledge to the contrary, and that the company, under these circumstances, was estopped from denying it was selling rabbits. That being so, the supreme court said that the same rules of law applied as if the seller of the rabbits was, in fact, defendant's agent.

Another question presented was whether the trial court had erred in charging that the violation of section 12760, General Code, constituted negligence per se. That section provided that whoever sold, offered for sale, or had in possession with intent to sell, diseased, corrupted, adulterated, or unwholesome provisions without making the condition thereof known to the buyer should be penalized. The supreme court took the view that the rule of law applied in a prior case also applied in the instant case. In such earlier case it was held (*a*) that the violation of the State pure food laws by the sale of unwholesome meat was negligence per se and could be the basis of recovery for damages by the user of such unwholesome meat who suffered injury proximately resulting therefrom, provided the user was not himself guilty of negligence in the care, preparation, cooking, or in any other manner which contributed directly to his injury, and (*b*) that lack of intent to violate the law or ignorance of the condition of the meat at the time it was sold was no defense.

The judgment for the plaintiff was affirmed.

DEATHS DURING WEEK ENDED JUNE 14, 1941

[From the Weekly Mortality Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended June 14, 1941	Corresponding week, 1940
Data from 88 large cities of the United States:		
Total deaths	7,776	7,956
Average for 3 prior years	7,755	
Total deaths, first 24 weeks of year	214,534	216,208
Deaths per 1,000 population, first 24 weeks of year, annual rate	12.5	12.6
Deaths under 1 year of age	511	520
Average for 3 prior years	494	
Deaths under 1 year of age, first 24 weeks of year	12,609	12,215
Data from industrial insurance companies:		
Policies in force	64,445,165	65,298,017
Number of death claims	11,685	12,063
Death claims per 1,000 policies in force, annual rate	9.5	9.7
Death claims per 1,000 policies, first 24 weeks of year, annual rate	10.2	10.3

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED JUNE 21, 1941

Summary

A sharp rise occurred in the incidence of poliomyelitis during the current week, with 67 cases reported for the country as a whole as compared with 26 for the preceding week. An increase of one or more cases was recorded in all geographic areas except the Middle Atlantic, the largest being for the South Atlantic States, which reported 28 cases as compared with 5 last week. The following named States reported the most significant increases and the largest numbers of cases: Florida, from 3 to 15; Georgia, from 0 to 9; Illinois, from 3 to 7; South Carolina, from 1 to 3; and Mississippi, from 2 to 4. California reported 7 cases as compared with 6 last week. The local distribution of the cases in Florida is not available. None was reported from Miami.

The total number of cases of poliomyelitis for the current week is slightly above the 5-year (1936–40) median (51). For the corresponding week of 1939 and 1937, 83 and 82 cases were reported, respectively. The total number of cases reported to date this year (first 25 weeks) is 636, as compared with a cumulative 5-year median of 657.

The incidence of measles declined in all geographic areas. A total of 16,194 cases was reported as compared with 21,420 for the preceding week. Of 48 cases of meningococcus meningitis, 6 cases were reported in New York, 4 each in Massachusetts, Ohio, and West Virginia, and 3 each in Maryland, Oregon, and California. A total of 32 cases of Rocky Mountain spotted fever was reported, as compared with 23 cases for the preceding week, and 46 cases of endemic typhus fever (18 in Texas, 10 in Alabama, 7 in Georgia, and 5 each in Florida and Louisiana) as compared with 50 last week.

The death rate for the current week in 88 major cities in the United States is 10.9 per 1,000 population, the same as for the preceding week. The 3-year (1938–40) average for the corresponding week is 10.5. The cumulative rate to date this year (first 25 weeks) is 12.4, as compared with 12.5 for the corresponding period of 1940.

Telegraphic morbidity reports from State health officers for the week ended June 21, 1941, and comparison with corresponding week of 1940 and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none were reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median, 1936–40	Week ended—		Median, 1936–40	Week ended—		Median, 1936–40	Week ended—		Median, 1936–40
	June 21, 1941	June 22, 1940		June 21, 1941	June 22, 1940		June 21, 1941	June 22, 1940		June 21, 1941	June 22, 1940	
NEW ENG.												
Maine	0	0	1		6		111	317	143	0	0	0
New Hampshire	0	0	0				3	18	18	0	0	0
Vermont	0	0	0				47	6	97	0	0	0
Massachusetts	3	3	2				759	1,164	711	4	0	1
Rhode Island	0	1	1				1	118	43	0	0	0
Connecticut	0	1	3	2	1	1	422	13	69	0	0	0
MID. ATL.												
New York	13	9	30		[1] 7	[1] 4	1,830	832	1,146	6	1	4
New Jersey	4	8	8	2	1	3	986	933	647	1	0	1
Pennsylvania	9	7	15				2,379	463	587	0	4	7
E. NO. CEN.												
Ohio [2]	15	16	16	3	11	8	1,280	40	217	4	1	1
Indiana [2]	3	0	5	3	2	2	218	12	12	0	3	1
Illinois	25	21	32	6	2	9	598	217	217	1	1	3
Michigan [2]	4	4	8		8	1	960	508	288	0	0	1
Wisconsin	4	4	4	28	9	13	1,222	954	400	0	0	1
W. NO. CEN.												
Minnesota	0	0	2			1	16	65	91	0	0	0
Iowa [2]	1	10	3	1			126	141	84	0	1	0
Missouri [2]	1	1	7		2	9	238	16	16	1	0	0
North Dakota	0	1	1	2		2	13	4	4	0	0	0
South Dakota	1	0	0				2	3	2	0	0	0
Nebraska	1	1	1				6	17	19	0	0	0
Kansas	7	4	5			1	152	225	54	0	0	0
SO. ATL.												
Delaware [2]	0	0	0				24	2	3	0	0	0
Maryland [2 3]	4	1	3	4	2	1	366	1	81	3	0	2
Dist. of Col	1	0	3				111	3	43	1	0	1
Virginia	8	5	6	16	22		528	138	138	2	3	3
West Virginia [2 3]	2	3	4	7	3	5	453	20	40	4	1	1
North Carolina	7	4	9	1			719	84	192	1	0	2
South Carolina	0	6	4	111	110	52	270	18	19	0	0	1
Georgia [4]	7	2	3	27	2		196	53	42	9	0	0
Florida [4]	2	1	4	9		1	50	32	13	1	0	0
E. SO. CEN.												
Kentucky	2	4	3		12	6	246	102	63	1	0	3
Tennessee	3	0	3	15	9	10	178	50	48	0	0	1
Alabama [4]	1	7	7	9	1	5	89	72	47	0	2	2
Mississippi [3 4]	3	1	3							1	1	1
W. SO. CEN.												
Arkansas	4	6	1	7	10	4	156	17	11	0	1	0
Louisiana [4]	1	3	10	2	19	9	3	2	8	0	1	1
Oklahoma	3	1	2	10	6	14	84	10	20	0	0	1
Texas [4]	13	20	20	237	80	80	489	379	174	2	1	1
MOUNTAIN												
Montana [2]	1	1	0	1			9	49	49	0	0	0
Idaho [2]	0	0	0				8	9	18	0	1	0
Wyoming [2]	4	0	0		2		5	8	5	0	0	0
Colorado [2]	7	15	5	12	1		108	44	46	0	0	0
New Mexico	1	1	3				82	62	16	0	0	0
Arizona	2	2	2	47	21	18	81	43	12	0	1	0
Utah [2 3]	0	3	0	1			43	204	81	0	0	0
Nevada	0						0			0		
PACIFIC												
Washington	0	2	1				12	141	141	0	0	0
Oregon	1	8	1	4		8	38	127	34	3	0	0
California	13	15	22	[5] 842	56	20	477	174	511	3	0	2
Total	181	202	292	1,409	405	437	16,194	7,910	7,968	48	23	44
25 weeks	6,395	7,629	11,359	594,479	166,266	149,068	788,425	201,321	246,888	1,172	957	1,857

See footnotes at end of table.

Telegraphic morbidity reports from State health officers for the week ended June 21, 1941, and comparison with corresponding week of 1940 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever		
	Week ended—		Median, 1936–40	Week ended—		Median, 1936–40	Week ended—		Median, 1936–40	Week ended—		Median, 1936–40
	June 21, 1941	June 22, 1940		June 21, 1941	June 22, 1940		June 21, 1941	June 22, 1940		June 21, 1941	June 22, 1940	
NEW ENG.												
Maine	0	0	0	3	7	7	0	0	0	0	2	1
New Hampshire	0	0	0	2	1	5	0	0	0	0	0	0
Vermont	1	0	0	2	3	3	0	0	0	3	1	0
Massachusetts	0	1	1	139	81	133	0	0	0	4	1	1
Rhode Island	0	0	0	5	0	11	0	0	0	1	3	1
Connecticut	1	0	0	29	36	36	0	0	0	2	2	1
MID. ATL.												
New York	0	0	1	316	328	328	0	0	0	11	7	10
New Jersey	1	0	0	132	161	70	0	0	0	2	0	2
Pennsylvania	1	0	0	172	163	174	0	0	0	7	8	8
E. NO. CEN.												
Ohio [2]	3	1	1	131	117	92	0	0	0	4	5	5
Indiana [2]	0	1	1	24	23	32	0	3	6	4	2	4
Illinois	7	1	1	156	317	247	5	14	9	7	4	7
Michigan [3]	1	5	1	242	148	283	0	1	1	4	3	2
Wisconsin	0	0	0	54	67	84	1	0	2	0	2	2
W. NO. CEN.												
Minnesota	2	1	1	23	26	48	0	1	8	0	0	0
Iowa [2]	0	1	0	14	21	23	2	2	17	2	2	2
Missouri [2]	0	1	0	30	11	25	0	0	2	0	16	6
North Dakota	0	0	0	1	12	13	0	0	1	0	0	0
South Dakota	1	0	0	2	7	6	0	1	1	1	0	0
Nebraska	0	1	0	9	11	11	0	1	5	0	1	0
Kansas	0	0	0	18	16	33	0	0	3	0	3	3
SO. ATL.												
Delaware [2]	0	0	0	6	4	1	0	0	0	0	1	0
Maryland [2 3]	0	1	0	29	19	19	0	0	0	0	1	3
Dist. of Col	0	1	0	6	6	6	0	0	0	0	1	0
Virginia	0	2	2	7	5	11	0	0	0	1	3	6
West Virginia [2 3]	0	1	1	9	15	15	0	0	1	2	3	4
North Carolina	1	1	1	13	9	13	0	0	0	3	5	9
South Carolina	3	0	0	2	3	2	0	0	0	6	4	12
Georgia [4]	9	1	1	8	6	8	0	0	0	15	17	30
Florida [4]	15	0	1	4	1	3	0	0	0	2	2	2
E. SO. CEN.												
Kentucky	1	2	1	42	24	15	3	0	0	3	7	11
Tennessee	0	0	1	15	23	10	2	0	0	9	5	16
Alabama [4]	3	0	5	4	9	4	0	1	0	3	9	9
Mississippi [3 4]	4	0	0	1	4	4	0	1	1	2	2	8
W. SO. CEN.												
Arkansas	0	0	0	2	4	6	0	4	3	10	6	9
Louisiana [4]	1	1	1	6	5	5	0	0	0	11	23	22
Oklahoma	1	1	1	3	8	9	0	0	3	4	5	10
Texas [4]	2	3	1	18	18	27	0	5	3	11	28	26
MOUNTAIN												
Montana [2]	0	0	0	12	5	8	0	0	1	2	1	1
Idaho [2]	0	0	0	1	6	6	1	0	0	1	2	1
Wyoming [2]	1	0	0	4	3	3	0	0	1	0	0	0
Colorado [2]	0	0	0	10	17	18	0	3	1	0	2	2
New Mexico	0	0	0	5	0	9	0	0	0	1	1	2
Arizona	1	0	0	3	3	3	2	0	0	3	4	3
Utah [2 3]	0	0	0	2	2	12	0	0	0	0	0	1
Nevada	0	----	----	0	----	----	0	----	----	0	----	----
PACIFIC												
Washington	0	9	0	10	29	25	1	0	0	0	2	2
Oregon	0	0	0	7	6	23	1	2	3	1	2	2
California	7	15	9	112	75	107	1	1	7	6	11	10
Total	67	51	51	1,845	1,865	2,168	19	40	141	148	209	271
25 weeks	636	697	657	85,449	111,454	128,743	1,084	1,725	7,219	2,249	2,451	3,370

See footnotes at end of table.

Telegraphic morbidity reports from State health officers for the week ended June 21, 1941, and comparison with corresponding week of 1940—Con.

Division and State	Whooping cough	
	Week ended—	
	June 21, 1941	June 22, 1940
NEW ENG.		
Maine	22	13
New Hampshire	2	10
Vermont	21	15
Massachusetts	188	116
Rhode Island	20	5
Connecticut	49	54
MID. ATL.		
New York	283	300
New Jersey	90	94
Pennsylvania	250	301
E. NO. CEN.		
Ohio [2]	330	204
Indiana [2]	13	24
Illinois	102	93
Michigan [3]	0	207
Wisconsin	123	92
W. NO. CEN.		
Minnesota	70	34
Iowa [2]	24	44
Missouri [2]	12	30
North Dakota	16	13
South Dakota	1	1
Nebraska	6	19
Kansas	156	56
SO. ATL.		
Delaware [2]	7	1
Maryland [2 3]	75	148
Dist. of Col.	10	4
Virginia	103	52
West Virginia [2 3]	49	33
North Carolina	155	155
South Carolina	168	8
Georgia [4]	23	20
Florida [4]	10	9
E. SO. CEN.		
Kentucky	52	75
Tennessee	78	31
Alabama [4]	40	19
Mississippi [3 4]	------	------
W. SO. CEN.		
Arkansas	31	31
Louisiana [4]	16	32
Oklahoma	12	34
Texas [4]	401	389
MOUNTAIN		
Montana [3]	31	1
Idaho [2]	18	9
Wyoming [3]	5	7
Colorado [2]	162	24
New Mexico	16	17
Arizona	55	11
Utah [2 3]	87	159
Nevada	0	------
PACIFIC		
Washington	61	63
Oregon	18	31
California	658	368
Total	4,139	3,426
25 weeks	115,118	80,316

[1] New York City only.
[2] Rocky Mountain spotted fever, week ended June 21, 1941, 32 cases, as follows: Ohio, 1; Indiana, 1; Iowa, 1; Missouri, 1; Delaware, 1; Maryland, 3; West Virginia, 1; Montana, 10; Idaho, 1; Wyoming, 8; Colorado, 2; Utah, 2.
[3] Period ended earlier than Saturday.
[4] Typhus fever, week ended June 21, 1941, 46 cases, as follows: Georgia, 7; Florida, 5; Alabama, 10; Mississippi, 1; Louisiana, 5; Texas, 18.
[5] Delayed reports.

PLAGUE INFECTION IN FLEAS FROM GROUND SQUIRRELS IN KERN COUNTY, CALIF.

Under date of June 11, 1941, Dr. N. E. Wayson, Medical Officer in Charge, Plague Suppressive Measures, San Francisco, Calif., reported plague infection proved, by animal inoculation and cultures, in a pool of 91 fleas from 5 ground squirrels, *C. beecheyi*, submitted to the laboratory on May 23, 1941, from a ranch 1 mile south of Cummings Valley School, Kern County, Calif.

WEEKLY REPORTS FROM CITIES

City reports for week ended June 7, 1941

This table summarizes the reports received weekly from a selected list of 140 cities for the purpose of showing a cross section of the current urban incidence of the communicable diseases listed in the table.

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Data for 90 cities:											
5-year average	109	42	21	3,792	372	1,297	14	367	31	1,212	-----
Current week [1]	50	48	12	6,694	285	979	0	357	31	1,445	-----
Maine:											
Portland	0	-----	0	1	0	1	0	0	0	1	18
New Hampshire:											
Concord	0	-----	0	0	0	2	0	0	0	0	9
Nashua	0	-----	0	0	0	0	0	0	0	6	7
Vermont:											
Barre	0	-----	0	0	0	0	0	0	0	0	3
Burlington	1	-----	0	1	0	0	0	0	0	0	9
Rutland	0	-----	0	0	0	0	0	0	0	0	3
Massachusetts:											
Boston	1	-----	0	249	0	69	0	12	1	76	197
Fall River	1	-----	0	2	2	1	0	0	0	4	31
Springfield	0	-----	0	70	1	14	0	2	0	13	43
Worcester	0	-----	0	29	2	5	0	0	0	0	57
Rhode Island:											
Pawtucket	1	-----	0	0	0	0	0	0	0	5	14
Providence	0	-----	0	0	1	2	0	2	0	18	44
Connecticut:											
Bridgeport	0	-----	0	24	0	2	0	2	0	2	34
Hartford	0	-----	0	4	1	8	0	1	0	2	35
New Haven	0	-----	0	6	1	9	0	0	1	2	30
New York:											
Buffalo	0	-----	0	46	19	28	0	5	0	14	152
New York	22	7	2	1,139	45	224	0	72	5	118	1,345
Rochester	0	-----	0	205	3	2	0	0	1	23	62
Syracuse	0	-----	0	11	3	2	0	0	1	28	42
New Jersey:											
Camden	2	-----	0	6	0	5	0	0	0	1	34
Newark	0	-----	0	52	5	8	0	8	0	16	116
Trenton	0	-----	0	66	0	5	0	4	0	1	42
Pennsylvania:											
Philadelphia	2	1	1	282	16	94	0	24	3	67	438
Pittsburgh	2	1	0	951	8	20	0	3	1	37	161
Reading	0	-----	0	135	1	6	0	0	0	2	17
Scranton	0	-----	-----	69	-----	1	0	-----	0	0	-----
Ohio:											
Cincinnati	1	-----	0	19	2	3	0	7	0	6	134
Cleveland	0	1	0	28	6	43	0	8	1	81	170
Columbus	1	-----	0	43	3	10	0	0	0	17	80
Toledo	0	-----	0	521	1	0	0	5	0	33	92
Indiana:											
Anderson	0	-----	0	9	1	0	0	0	0	0	7
Fort Wayne	0	-----	0	9	1	0	0	0	0	4	20
Indianapolis	1	-----	0	298	10	4	0	7	0	19	126
Muncie	0	-----	0	24	1	3	0	0	0	2	11
South Bend	0	-----	0	22	0	0	0	0	0	0	8
Terre Haute	0	-----	0	3	1	1	0	0	0	0	17
Illinois:											
Alton	0	-----	0	9	0	0	0	0	1	0	1
Chicago	5	1	0	161	22	98	0	38	0	31	650
Elgin	0	-----	0	4	1	1	0	0	0	1	7
Springfield	0	-----	0	47	0	1	0	0	0	0	20
Michigan:											
Detroit	1	2	0	435	12	104	0	18	0	94	263
Flint	0	-----	0	28	4	6	0	0	0	19	19
Grand Rapids	0	-----	0	104	0	9	0	0	0	10	28
Wisconsin:											
Kenosha	0	-----	0	33	0	3	0	0	0	0	10
Madison	0	-----	0	10	0	2	0	0	0	2	9
Milwaukee	1	1	1	617	1	23	0	1	0	46	113
Racine	0	-----	0	52	0	5	0	0	0	6	7
Superior	0	-----	0	1	0	0	0	0	0	16	8

[1] Figures for Raleigh, Boise, and mortality figures for Salt Lake City estimated; reports not received.

City reports for week ended June 7, 1941—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Minnesota:											
Duluth	0		0	0	3	0	0	0	0	23	32
Minneapolis	0		0	8	1	16	0	0	2	15	105
St. Paul	0	1	1	1	1	4	0	3	0	17	60
Iowa:											
Cedar Rapids	0			6		0	0		0	0	
Davenport	0			0		0	0		0	0	
Des Moines	0			2		2	0		0	2	34
Sioux City	0			4		2	0		0	11	
Waterloo	0			38		0	0		0	2	
Missouri:											
Kansas City	0		0	110	2	6	0	3	0	17	76
St. Joseph	0		0	10	5	0	0	3	0	1	26
St. Louis	0		0	217	4	32	0	5	0	28	190
North Dakota:											
Fargo	0		0	0	0	0	0	0	0	21	9
Grand Forks	0			0		0	0		0	0	
Minot	0			6		0	0		0	1	9
South Dakota:											
Aberdeen	0			0		0	0		0	1	
Sioux Falls	0			0		3	0		0	0	7
Nebraska:											
Lincoln	0			3		1	0		0	2	
Omaha	0		0	7	6	3	0	1	0	0	49
Kansas:											
Lawrence	0		0	2	0	0	0	0	0	4	7
Topeka	0		0	26	2	0	0	0	0	27	16
Wichita	0	1	0	7	0	0	0	1	0	4	21
Delaware:											
Wilmington	0		0	8	3	5	0	0	0	0	32
Maryland:											
Baltimore	1	3	2	294	9	11	0	14	0	81	187
Cumberland	0		0	2	0	0	0	0	0	0	13
Frederick	0		0	0	0	0	0	0	0	0	4
Dist. of Col.:											
Washington	0		0	199	8	8	0	9	0	11	158
Virginia:											
Lynchburg	0		0	24	0	0	0	1	2	1	10
Norfolk	0		0	20	0	0	0	1	0	3	26
Richmond	0		1	71	2	0	0	0	0	0	57
Roanoke	0		0	7	0	1	0	0	0	0	12
West Virginia:											
Charleston	0		0	0	3	0	0	1	0	0	26
Huntington	0			5		0	0		0	0	
Wheeling	0		0	43	3	3	0	0	0	3	19
North Carolina:											
Gastonia	0			2		1	0		0	0	
Raleigh											
Wilmington	0		0	9	0	0	0	0	0	25	9
Winston-Salem	0		0	10	2	0	0	1	0	6	15
South Carolina:											
Charleston	0		0	0	0	0	0	3	1	1	19
Florence	0		0	0	2	0	0	0	0	7	10
Greenville	0		0	3	2	0	0	0	0	1	13
Georgia:											
Atlanta	1		1	44	2	2	0	4	1	1	69
Brunswick	0		0	4	0	0	0	0	0	0	5
Savannah	0	1	0	11	0	1	0	3	0	0	30
Florida:											
Miami	0		0	4	1	0	0	1	3	6	37
St. Petersburg	0		0	3	1	0	0	1	1	0	20
Tampa	0		0	0	0	0	0	1	0	2	21
Kentucky:											
Ashland	0		0	7	0	0	0	0	0	5	
Covington	0		0	0	1	0	0	0	0	0	11
Lexington	0		0	0	1	0	0	2	0	0	15
Louisville	0		0	428	5	24	0	4	0	9	57
Tennessee:											
Knoxville	1		0	20	1	4	0	1	1	1	27
Memphis	0	6	0	70	2	0	0	1	0	4	73
Nashville	0		1	21	2	8	0	2	0	12	50
Alabama:											
Birmingham	0	3	0	6	3	2	0	4	0	3	61
Mobile	0		0	0	0	0	0	1	0	0	20
Montgomery	0			0		0	0		0	0	

City reports for week ended June 7, 1941—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Arkansas:											
Fort Smith	1	----	----	0	----	0	0	----	0	0	----
Little Rock	0	----	0	3	2	0	0	4	2	0	49
Louisiana:											
Lake Charles	0	----	0	1	0	0	0	0	0	0	6
New Orleans	1	----	0	5	4	2	0	12	2	0	106
Shreveport	0	----	0	0	4	2	0	3	3	3	27
Oklahoma:											
Oklahoma City	0	1	0	7	3	0	0	1	0	2	45
Tulsa	0	----	0	38	1	1	0	0	0	2	10
Texas:											
Dallas	1	----	0	18	5	0	0	6	0	1	61
Fort Worth	0	----	0	2	1	1	0	0	0	0	34
Galveston	0	----	0	0	1	4	0	0	0	0	15
Houston	0	----	0	3	8	4	0	8	2	1	98
San Antonio	1	2	1	1	2	1	0	9	0	2	79
Montana:											
Billings	0	----	0	0	1	0	0	0	0	0	5
Great Falls	0	----	0	3	0	1	0	0	0	1	6
Helena	0	----	0	4	0	0	0	0	0	0	2
Missoula	0	----	0	0	1	0	0	0	0	0	8
Idaho:											
Boise	----	----	----	----	----	----	----	----	----	----	----
Colorado:											
Colorado Springs	0	----	0	6	2	6	0	0	0	2	9
Denver	3	8	1	154	4	2	0	6	0	105	82
Pueblo	0	----	0	10	1	2	0	0	0	13	5
New Mexico:											
Albuquerque	0	----	0	3	0	0	0	2	0	0	11
Arizona:											
Phoenix	0	31	----	0	----	0	0	----	0	15	----
Utah:											
Salt Lake City	0	----	----	3	----	3	0	----	0	15	----
Washington:											
Seattle	1	----	0	0	3	1	0	2	0	29	104
Spokane	0	----	0	4	2	3	0	1	0	8	38
Tacoma	0	----	0	6	1	3	0	0	0	22	32
Oregon:											
Portland	1	----	0	0	5	4	0	2	0	0	89
Salem	0	----	----	1	----	0	0	----	0	0	----
California:											
Los Angeles	0	8	0	61	4	25	0	18	2	63	318
Sacramento	0	1	0	4	3	2	0	2	0	41	39
San Francisco	1	----	0	2	4	5	0	10	0	31	141

State and city	Meningitis, meningococcus		Poliomyelitis cases	State and city	Meningitis, meningococcus		Poliomyelitis cases
	Cases	Deaths			Cases	Deaths	
Massachusetts:				Michigan:			
Boston	3	0	0	Detroit	1	0	0
New York:				Missouri:			
Buffalo	1	0	0	St. Joseph	0	1	0
New York	1	0	2	Maryland:			
New Jersey:				Baltimore	3	0	1
Camden	0	1	0	Louisiana:			
Pennsylvania:				Shreveport	0	1	0
Scranton	1	1	0	Texas:			
Ohio:				Dallas	0	1	0
Toledo	1	1	0	California:			
				Los Angeles	1	1	3

Encephalitis, epidemic or lethargic.—Cases: Philadelphia, 1. Deaths: New York, 1; Chicago, 1; Louisville, 1; Albuquerque, 1; Sacramento, 1.
Pellagra.—Cases: Philadelphia, 1; Savannah, 4; Dallas, 2; Sacramento, 1.
Rabies in man.—Deaths: Wilmington, N. C., 1.
Typhus fever.—Cases: Savannah, 1; Miami, 3.

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended May 24, 1941.—During the week ended May 24, 1941, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Cerebrospinal meningitis		6		7	9			2	6	30
Chickenpox		33		104	130	65	12	40	29	413
Diphtheria		10	1	16	2	2	2			33
Dysentery				6						6
Influenza		8			2				6	16
Measles		76	64	[illegible]	1,313	97	26	33	187	2,402
Mumps		1	1	262	149	19	53	5	18	508
Pneumonia		8			4	1			9	22
Scarlet fever	1	24	1	151	129	8	11	4	20	349
Smallpox							1			1
Tuberculosis		4	7	126	50	56	1			244
Typhoid and paratyphoid fever				13	2					15
Whooping cough				117	145	1	1	9	27	300

CUBA

Habana—Communicable diseases—4 weeks ended May 31, 1941.—During the 4 weeks ended May 31, 1941, certain communicable diseases were reported in Habana, Cuba, as follows:

Disease	Cases	Deaths
Diphtheria	18	2
Malaria	1	
Tuberculosis		2
Typhoid fever	21	

SWITZERLAND

Communicable diseases—March 1941.—During the month of March 1941, cases of certain communicable diseases were reported in Switzerland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis	31	Mumps	101
Chickenpox	217	Paratyphoid fever	3
Diphtheria	72	Poliomyelitis	4
German measles	158	Scarlet fever	288
Influenza	108	Tuberculosis	255
Lethargic encephalitis	1	Typhoid fever	8
Malaria	1	Undulant fever	8
Measles	369	Whooping cough	157

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

From medical officers of the Public Health Service, American consuls, International Office of Public Health, Pan American Sanitary Bureau, health section of the League of Nations, and other sources. The reports contained in the following tables must not be considered as complete or final as regards either the list of countries included or the figures for the particular countries for which reports are given.

CHOLERA

[C indicates cases; D, deaths]

NOTE.—Since many of the figures in the following tables are from weekly reports, the accumulated totals are for approximate dates.

Place		January–March 1941	April 1941	May 1941—week ended—				
				3	10	17	24	31
ASIA								
China:								
Canton[1]								
Hong Kong	C	567	117	28	35	32	-----	-----
Macao	C	-----	-----	10	16	29	49	58
India:								
Calcutta	C	1,164	504	-----	-----	-----	-----	-----
Rangoon	C	28	4	-----	10	-----	-----	-----
India (French)	C	10	-----	-----	-----	-----	-----	-----

[1] A report dated May 21, 1941, states that up to May 19, 52 cases of cholera with 27 deaths were reported in Canton, China.

PLAGUE

[C indicates cases; D, deaths]

AFRICA								
Belgian Congo	C	1	-----	-----	-----	-----	-----	-----
British East Africa:								
Kenya	C	10	-----	-----	-----	-----	-----	-----
Uganda	C	41	-----	-----	-----	-----	-----	-----
Madagascar	C	172	11	-----	-----	-----	-----	[1] 8
Morocco	C	617	181	71	47	74	109	45
Tunisia: **Tunis**	C	2	-----	-----	-----	-----	-----	-----
Union of South Africa	C	33	3	-----	-----	-----	-----	-----
ASIA								
Dutch East Indies:								
Java ar Madura	C	252	-----	-----	-----	-----	-----	-----
West Java	C	162	-----	-----	-----	-----	-----	-----
India:								
Calcutta	C	3	-----	-----	-----	-----	-----	-----
Rangoon	C	2	-----	2	-----	-----	-----	-----
Thailand: Lampang Province	C	-----	1	-----	-----	-----	-----	-----
SOUTH AMERICA								
Argentina: Cordoba Province	C	1	-----	-----	-----	-----	-----	-----
Peru:								
Lambayeque Department	C	2	-----	-----	-----	-----	-----	-----
Libertad Department	C	6	-----	-----	-----	-----	-----	-----
Lima Department	C	5	-----	-----	-----	-----	-----	-----
OCEANIA								
Hawaii Territory: Plague-infected rats		10	1	4	6	1	9	-----
New Caledonia	C	7	-----	-----	-----	-----	-----	-----

[1] For the month of May.

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

SMALLPOX

[C indicates cases; D, deaths]

Place		January–March 1941	April 1941	May 1941—week ended—				
				3	10	17	24	31
AFRICA								
Algeria	C	79	24	11	----	----	----	----
British East Africa	C	9	----	----	----	----	----	----
Dahomey	C	351	16	----	----	----	----	[1] 85
French Guinea	C	20	3	----	----	----	----	[1] 22
Ivory Coast	C	21	9	----	----	----	----	----
Morocco	C	27	4	----	----	----	----	----
Nigeria	C	323	74	----	----	----	----	----
Niger Territory	C	124	71	----	----	----	----	[1] 26
Portuguese East Africa	C	9	----	----	----	----	----	----
Rhodesia: Southern	C	86	----	----	----	----	----	----
Senegal	C	30	13	----	----	----	----	[1] 9
Sierra Leone	C	----	15	----	----	----	----	----
Sudan (Anglo-Egyptian)	C	5	2	----	----	----	----	----
Sudan (French)	C	14	5	----	----	----	----	----
ASIA								
Ceylon [2]	C	----	6	----	----	----	----	----
China	C	114	24	6	10	6	1	2
Chosen	C	[3] 207	----	----	----	----	----	----
India	C	9,803	104	----	----	----	----	----
India (French)	C	4	----	----	----	----	----	----
India (Portuguese)	C	44	----	----	----	----	----	----
Indochina (French)	C	325	180	----	----	----	----	[1] 197
Iran	C	4	----	----	----	----	----	----
Iraq	C	892	----	----	----	----	----	----
Japan	C	92	10	----	----	----	----	----
Straits Settlements	C	1	----	----	----	----	----	----
Syria	C	1	----	----	----	----	----	----
Thailand	C	80	16	30	10	9	43	23
EUROPE								
France	C	1	----	----	----	----	----	----
Portugal	C	12	6	1	----	----	1	----
Spain	C	97	1	----	----	----	----	----
NORTH AMERICA								
Canada	C	3	10	----	9	----	----	----
Cuba	C	----	1	----	----	----	----	----
Dominican Republic	C	2	----	----	----	----	----	----
Guatemala	C	3	1	----	----	----	----	----
Mexico	C	18	----	----	----	----	----	----
SOUTH AMERICA								
Colombia	C	220	3	1	----	----	----	----
Uruguay	C	7	----	----	----	----	----	----
Venezuela (alastrim)	C	47	24	----	----	----	----	----

[1] For the month of May.
[2] A report dated May 16, 1941, states that within the last few weeks 20 cases of smallpox were reported in Colombo, Ceylon, and 12 cases in other localities of Ceylon.
[3] For the month of January.

WORLD DISTRIBUTION OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

TYPHUS FEVER

[C indicates cases; D, deaths]

Place		January–March 1941	April 1941	May 1941—week ended— 3	10	17	24	31
AFRICA								
Algeria	C	2,080	1,047					[1] 1,255
Egypt	C	355						
Morocco	C	139	102	29	22	44		49
Sierra Leone	C	4	1					
Tunisia	C	994	712	201	217	199	254	
Union of South Africa	C	113	2					
ASIA								
China	C	55	30			2		
Chosen	C	[2] 5						
Iran	C	60						
Iraq	C	13						
Japan	C	125	34					
Straits Settlements	C	2						
EUROPE								
Bulgaria	C	71	9	21		14		
Germany	C	355	199	47	49			
Greece	C	7						
Hungary	C	91	45	29	34		34	
Irish Free State	C	9	4				13	
Poland	C	145						
Rumania	C	439	47	10	20		9	17
Spain	C	500	856			255		
Switzerland	C	2						
Turkey	C	[3] 175						
Yugoslavia	C	78						
NORTH AMERICA								
Guatemala	C	82	10					
Mexico	C	18	2		1	1		
Panama Canal Zone	C	3						
SOUTH AMERICA								
Chile	C	50						
Ecuador	C	29	21					
Venezuela	C	20	6					
OCEANIA								
Australia	C	6	1					
Hawaii Territory	C	3	7	1	1			1

[1] For the month of May.
[2] For the month of January
[3] For January and February.

YELLOW FEVER

[C indicates cases; D, deaths]

Place								
AFRICA								
French Equatorial Africa	C	2						
Gold Coast	C		1					
Ivory Coast	C	[1] 3						
Spanish Guinea	D			4				
SOUTH AMERICA [2]								
Colombia:								
Antioquia Department	D	1						
Boyaca Department	D	3	1					
Intendencia of Meta	D	1						
Santander Department	D	2						
Tolima Department	D	1						

[1] Includes 2 suspected cases.
[2] All yellow fever reported in South America is jungle type unless otherwise stated.

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